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THE SHATTUCK LECTURE*

THE STUDY OF IMMUNITY IN ITS RELATION TO THE PROBLEM OF PRACTICAL MEDICINE

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I.

It is an unfortunate, though probably inevitable circumstance that so many of the sciences which have as ultimate objectives the solution of the problems of disease should, so often and for such long periods, develop in directions which seem to carry them completely out of the spheres of practical medicine. The reason why this must be so lies, obviously, in the complexity of the problems involved, since the ultimate complete understanding of even the simplest phenomenon in which living matter is concerned is still an unattained ambition; and the bridge of comprehension between the test tube experiment and the observation of the functional activities of cells and tissues must be spanned in many places with inference and hypothesis. In endeavoring to understand occurrences and trace mechanism, the worker travels long and solitary paths that often lead him far away from the contacts of practical application or even comprehensible expression in the terms of clinical medicine; and during these periods it often and naturally appears to the clinicians that the elaborate and expensive methods of science are sterile. This has been particularly true of immunology, owing to the fact that the various reactions by which the living body responds to invasion by lower forms of life are merely special instances of general biological phenomena which, to be properly comprehended, must be studied upon a broader plan than the mere observations possible at the bedside or in the animal experiment.

Nevertheless, it is true that the gap between investigators and clinicians has been a wider one than necessary. But it is narrowing—mainly, perhaps, because of the rapidly growing application of the results of immunological study to the diagnostic and therapeutic problems of medicine. Although as the science matures, greater insight extends the boundaries of the

unknown territory, yet, though growing at a slower ratio, knowledge gradually accumulates to such an extent that it begins materially to alter conceptions of infectious disease and, consequently, of practice.

In immunology there are certain principles about which we can be quite sure at the present time which underlie and give direction to investigative endeavors. They are simple conceptions and pitifully meager if considered in the light of the effort it has cost to attain them, but still so fundamental in their characterization of the reactions of living protoplasm that they should be clearly understood by all who deal with infectious disease under any circumstances.

It will be my endeavour in this talk to construct for you the bare trellises of basic fact and theory, very briefly; and then to apply the reasoning for which these facts and theories form the premises to a number of the problems which are engaging the efforts of investigators.

The tissue cells of the higher animals are normally prepared for direct contact only with materials concerned in the processes of nutrition essential to the maintenance of life. In the lower forms, where a single cell may contain within itself the complete functions of an independent living being, and where intracellular digestion is still a physiological process, and even in certain special cells of the higher animals—like the leucocytes and other phagocytic cells in which such atavistic capacities survive—the range is a wider one. But, in general, the materials which are carried to the tissue cells of higher animals under normal conditions are prepared by elaborate preliminary digestion. Proteins reach the cells as amino-acids; fats as glycerol, fatty acids and perhaps soaps; and the carbohydrates as simple sugars. These materials, with oxygen, water and various salts, comprise the substances necessary for cell metabolism. It is, however, inevitable that many other things may from time to time find their way into the circulation and come into contact with the cells, and such substances, though without metabolic value and often even harmful, may be able to establish either a chemical or physical relationship with the cell protoplasm.

Ehrlich conceived the cell as a "giant molecule," a homogeneous chemical system of enor-

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mous molecular weight, possessing a large number of side chains by union with which the various elements essential to metabolism became chemically related to the cell. The manifold nature of these side chains would imply capacity for union with many other substances not of metabolic importance but possessing chemical affinity for individual side chains. A conception of the cell more likely to correspond to the actual conditions is the one which Bayliss describes as "a complex of substances of various chemical natures, and in various states of aggregation, associated together by forces of surface tension, electrical charge, etc. In these the liquid state enables an elaborate play of forces to take place. Chemical reactions can evidently proceed simultaneously in different parts of the cell, so that there is some mechanism by which one part is at least temporarily isolated from another." Such heterogeneous systems, partitioned and probably surrounded by semi-permeable surface layers may be influenced by their environment in a number of ways. Varying concentration of many substances may affect them osmotically. Diffusible materials, harmful or otherwise, may enter the cells and there combine with cell constituents, or alter physical states. Non-diffusible substances—notably the proteins—may establish relations only with the cell surfaces, and this only, in all probability, when some sort of chemical relationship can be established between specific radicals of the colloidal substances and the surface of the cell.

There are, of course, many substances, both organic and inorganic, which may diffuse into a cell without causing noticeable physiological changes. And there are many colloidal substances that may, at times, get into the circulation and, having no capacity for chemical union with the cell membranes, circulate and are gradually eliminated without immunological consequence. We refer to such materials as mastic, gum acacia, gelatin and other so-called "non-antigenic" colloids. In immunology, however, we are concerned only with substances which, upon entrance into the circulation and contact with the cells, arouse responses which specifically alter subsequent reaction capacities of the cell for similar contacts. It is probable that the substances which do this are all capable of establishing at least temporary chemical union with some part of the cell. In complexity these substances range from materials as simple as arsenic, through the alkaloids, to the proteins themselves. The alteration in reaction capacity of the cells which these materials induce expresses itself either in the form of an increased susceptibility to the particular material or its antithesis, increased tolerance, which, in the case of bacterial substances, is spoken of as immunity.

The laws which govern the acquisition of

such specific changes in cellular reaction vary according to the chemical complexity of the substance involved, and such phenomena as the drug idiosyncrasies and tolerances represent a special and very obscure chapter of immunology, into which we cannot afford to enter at present. It is more than likely that the fundamental differences in mechanism which unquestionably distinguish drug idiosyncrasies and drug tolerances from analogous hypersusceptibilities and immunity in the cases of proteins and bacteria depend upon the fact that the drugs, being diffusible, enter the cells; and the processes which determine subsequent occurrences are essentially intracellular. That an immunological process of some kind is probably involved in these phenomena seems likely because mere enhancement of excretory functions cannot explain increased resistance. Indeed, it has been shown, at least in such cases as alcohol and morphine, that similar concentrations of the drug in the blood of normal and of habituated individuals cause a deeper state of narcosis in the normal subjects, a clear indication that some basic cellular resistance is involved. Thus, the fact that there are no so-called "antibodies" formed in the drug idiosyncrasies and some other comparable conditions, though of the greatest practical importance, may be a superficial rather than a fundamental distinction. These problems, however, form a special and quite unexplored branch of immunology, and we must limit ourselves in our present discussion to those phenomena in which the more complex materials, the proteins and some of their closely related derivatives, are involved.

When such substances are broken down by the intestinal enzymes before absorption, they reach the cell in a form in which they arouse no immunological reactions. When, on the other hand, such materials gain access to the circulation without preliminary cleavage, they may be regarded as chemical foreign bodies, whether or not they have undergone solution. Though unable to diffuse into the cells, there seems little doubt that they can establish a chemical union with the cells themselves. This follows from the mere fact that they arouse specific reaction; further than this, however, it is clear from the fact that the specificity of various proteins can be altered in a controllable way by chemical alteration. Thus, iodizing, methylizing, or in a number of ways attaching certain atom-groups to the protein molecule, has resulted in producing antigens which induce reactions specific only for the altered protein, indicating a definite relationship between chemical structure and antigenic specificity. The criteria, therefore, which determine whether or not a certain substance is or is not capable of arousing specific immunological reactions in the body or, in other words, is antigenic, seems to be, in the first place, large molecular size, in

the second, chemical capacity for union with the cell. Though we know little about the mystery of specificity, we do know that it depends upon definite chemical groups in the protein molecule, which, according to the studies of Landsteiner and others, in the case of the proteins, seem involved in the aromatic amino-acid constituents.

Contact of the body cell with such protein materials means, as we have said, subsequent changes in its capacity to react with them. This, in the case of the protein and bacterial substances, takes the form of what is called "antibody formation." While the term "antibody" is a convenient one, it must be understood that we really do not know what the so-called "antibodies" are. While it has been definitely shown that they do not lead to chemical change of the antigen and, therefore, are not to be regarded as enzymes in the usual sense, nevertheless, they probably represent an emergency apparatus for the disposal of non-diffusible chemical foreign bodies which get into the circulation without preliminary digestion. And, in this sense, bacterial infection may be regarded as the entrance of a self-multiplying foreign protein or protein-like substance, the antibody mechanism the specific part of the emergency provision for their disposal. The cells unite with the antigenic substances. If they remain uninjured, they react by the obscure process of antibody formation—which, in the language of fact, means merely that something has happened which enables the cells themselves to react more powerfully with the particular substance ("hypersusceptibility due to sessile antibodies"), or later manifests itself by the appearance in the plasma of substances which can specifically unite with the injected material,—a union which can be quantitatively measured in the test tube experiment (agglutination, precipitation, complement fixation, toxin-neutralization, etc.)—and this practically constitutes the bare bone of the basic occurrences. Cells which have once so reacted may take a long time or may never return entirely to normal in relation to the particular substance by which they have been stimulated to response. Thus the quasi-permanent immunity acquired to plague, cholera or typhoid, the hypersusceptibility or anaphylaxis to various proteins which remain throughout life, indicate a basic change which probably means a hair-trigger response to a specific stimulus which at first contact was slow and imperfect.

While I say that this is practically the total of our knowledge, I mean by that that these facts constitute the corner stones of a very elaborate structure of many details; and the naked statements as I have made them, to be fully accurate, would require much elaboration and many qualifications. It will be sufficient for our present purposes if we fully sense that they stimulate the body to "antibody pro-

duction," and that the study of the defense mechanism of the body consists almost entirely in attempts to understand the nature of the antigenic materials contained in the various bacteria, their selective toxicity, the antibodies which they induce and the mechanisms of the reactions which take place, within the body and in the test tube, between these two specifically related and often mutually neutralizing factors.

We are purposely omitting from this discussion the important problems of the purely cellular defences of the actively immunized body, partly for lack of time, mainly because these phenomena are of relatively less significance in connection with the passive therapeutic immunization or serum therapy to which we have chosen to give particular attention in this paper.

One of the most important distinctions to make in thinking of the various antigenic substances in nature is to remember that there are primarily toxic bacterial substances, like diphtheria toxin and tetanus toxin, which, like some of the enzyme-like poisons of animal and vegetable origin, snake venom and ricin, induce the formation of antibodies which specifically and by definite quantitative proportions neutralize the toxic action of the respective antigen. When these neutralizing substances appear in the circulation, they represent the antitoxins, and these antitoxins represent a response to certain soluble poisonous products of the bacteria, the true toxins, which,—though we may describe them by many minor properties,—are after all essentially recognized as true toxins only by their capacities to induce neutralizing antitoxin in the animal body. There are, however, other bacterial antigens not necessarily toxic, or perhaps toxic in a different way, which act more or less like the true non-toxic proteins,—horse serum, egg albumen, etc.—in the fact that they induce antibodies which appear to have no particular poison-neutralizing properties but, rather, act upon the bacterial cell by inducing agglutination, precipitation, complement fixation, and possess a certain amount of protective action when injected in the form of serum. These anti-bacterial antibodies, as distinguished from the antitoxins, have the property of uniting specifically with the bacterial cell and so altering its molecular equilibrium in suspension, its electrical properties and other more obscure conditions, that the cell is now subject to flocculation by electrolytes, is rendered susceptible to the action of complement and to phagocytosis. These various antibodies have been spoken of as the agglutinins, opsonins, etc., but are held by us to be one and the same, namely, a sensitizing antibody, union with which subjects the cell to these various demonstrable alterations.

Broadly speaking, therefore, the two important types of sera for therapeutic passive im-

munization which have been produced have been the antitoxic and the antibacterial. In the diseases in which the clinical picture has been dominated by the action of a true exotoxin and immunization of animals with such an exo-toxin has produced the neutralizing antitoxic substance, serum treatment has made satisfactory progress, since the therapeutic requirements have been completely met by the neutralization of the poison responsible for the symptoms. Some qualification of this is of course necessary in a condition like tetanus, where the poison is bound by nerve tissues and has become inaccessible to the antitoxin, but, at any rate, the limitations of serum therapy have been probably reached in this disease when a true antitoxic substance has been produced. In diseases in which, so far, no antitoxin-producing poisons have been found, the use of the antibacterial sera which, by agglutinating, phagocytosis-inducing and other direct antibacterial protective mechanisms have tended to aid the body in getting rid of invading organisms, therapy has been less satisfactory, because—in such cases—from animal experimentation we know that, even with high potency, the curative value of the sera is apparent to any extent only when the serum is given before infection together with the organisms or relatively soon after inoculation.

It is not our purpose to enter more deeply into the many experimental and theoretical discussions without which no thorough exposition of our problems can be made, nor would anything be gained by enumerating the practical achievements of immunological procedures which underlie current clinical practice. Our field is too large to permit of anything but a very careful choice of topics for any single discussion, and I have thought that probably the most profitable use I can make of our time would be to consider with you the immunological principles underlying a number of important infectious diseases. I have chosen the examples in such a way that they will permit me to illustrate the many differences of approach and the variations of types of immunity upon which rational experimentation and therapeutic deductions must be based.

II.

THE SCARLET FEVER PROBLEM

The brilliant advances recently made in our knowledge of scarlet fever have kept this subject very much before the minds of the physicians and it would be mere repetition to discuss it at any length. I speak of it, however, in order to emphasize some very important lessons that the immunologist has learned from this work and to discuss some of the theoretical questions, proper interpretation of which will exert much influence upon investigation of the next few years.

As early as 1902, von Pirquet, on the basis of agglutinations, asserted that a specific serological type of streptococcus was associated with scarlatina; and Moser prepared a serum by the immunization of horses with living cultures with which considerable therapeutic success was attained. Soon after this, unfortunately, the issue became clouded by the suspicion of filtrable virus as the primary invader, and etiological opinion was suspended and left much in the same condition in which the influenza question remains at the present day. Although, therefore, had we only known it, the problem was solved in all its essential points, it remained for recent American investigation to place the etiology and therapy of this disease upon a probably permanent basis. Comparative appraisals as to the relative credit to be given to the Dicks and to Dochez and his co-workers should properly disappear in the pleasure that the achievement as a whole must give anyone blessed with the capacity for admiration for a good job well done.

The Dicks have been studying this question since 1914, and during this time Bliss, Gordon and Tunnicliff adduced further facts which pointed to the existence of special serological strains in scarlet fever. In spite of the confusion which resulted from a number of doubtful experimental inoculations of monkeys and other animals, and in spite of discouragement with their first human inoculations, the Dicks finally, in 1923, succeeded in producing experimental scarlet fever in 1 out of 5 volunteers by swabbing the pharynx with cultures of a hemolytic streptococcus isolated from the finger of a nurse suffering from the disease. A confirmatory experiment was obtained with another culture soon after this and the etiological problem seemed satisfactorily solved.

In view of the relatively small areas of the body upon which the streptococcus is localized in all but the fulminating cases of scarlet fever, all views which attribute etiological importance to the hemolytic streptococcus were inevitably impelled to assume a powerful toxic factor in explaining the clinical picture. Subsequent developments are sufficiently familiar. The outstanding fact from the immunologist's point of view is that in scarlatinal streptococcus cultures there appear, in 5, 6 or 7 days, substances which produce various degrees of toxic reaction when injected intracutaneously into man; and that the serum of horses immunized by appropriate methods will neutralize the action of such culture filtrates. To this extent, then, the scarlet fever streptococcus appears similar to diphtheria and tetanus bacilli in apparently producing a substance of definite toxicity which, in a properly immunized animal, gives rise to neutralizing anti-substances. And it is along these lines of thought that the Dicks and Dochez have approached the problem with

a degree of success that has gradually eliminated doubt.

While these therapeutic successes, of course, offset in importance any differences of theory, it is important to thoroughly elucidate the mechanism of these occurrences both in order to improve the present methods and to utilize the facts in other directions. There are a number of differences between the so-called "Dick toxin" and other antitoxin-producing bacterial poisons, and there are a few matters in regard to the methods of antiserum production which will still require much immunological analysis before we can profit from these brilliant achievements to the fullest extent.

In the first place, the toxin itself is heat stable to a degree hitherto unknown in bodies of this type, except to a lesser degree in snake poison. It will remain active in most cases after boiling and, according to Anna Williams, some preparations will withstand such treatment for 30 minutes to one hour. The toxin, moreover, has little relationship to the invasiveness of the organisms. We have been able to kill rats with 0.5 to 1.0 c.c. of living cultures of the Dick strains, while 5 to 10 c.c. of the broth filtrate seemed to have no effects whatever.

The reactions on the skin, moreover, differ somewhat from the known toxin reactions, resembling in development, appearance and the speed of fading those which may be obtained with many bacterial filtrates and are usually interpreted as signs of allergy or hypersusceptibility. This point is particularly significant in the light of the fact that both Dochez and the writer, with Grinnell, have had no difficulty in sensitizing normal guinea pigs with streptococci so that upon later test they gave definite allergic skin reactions with Dick filtrate. Curiously enough, our own animals, upon continued treatment with streptococci, passed through the allergic state into one of immunity or de-sensitization, and Dochez succeeded in neutralizing the action of Dick filtrate upon such sensitized animals with the same serum which faded the rash of scarlatinal patients. Both of these facts should cause the thoughtful investigator to hesitate in forming a final conclusion regarding the immunological mechanism of the Dick reaction, particularly since the Dick filtrate is much more similar in heat resistance, method of production, etc. to tuberculin than it is to some of the classical exo-toxins.

In view of these considerations, we feel that no final decision concerning the nature of the Dick reaction nor its significance should be made until considerably more information is available in regard to its relationship to actual immunity to scarlet fever and the prospects of actively immunizing human beings by repeated injections of the filtrate. In both cases we are inclined to feel hopeful that a complete analogy with the Schick reaction and active immuniza-

tion in diphtheria may exist, but neither of these questions is as yet finally settled.

We discuss these points only to indicate that the nature of the Dick toxin, the mechanism of its action and the immunological principles involved in scarlet fever are matters that require much further investigation. Whatever the final solution may be, however, the important practical points which now seem to be settled beyond question are that by the immunization of horses with streptococcus filtrates, or, perhaps better, by the Dochez method, sera can be produced which exert a neutralizing action upon the filtrates, blanch the scarlatinal rash and have definite curative value for the disease. With these discoveries a new train of thought has been introduced in the principles of immunity as applied to the Gram positive cocci and perhaps to other organisms. Indeed, J. T. Parker has already discovered that certain strains of staphylococci will produce toxic substances that are quite potent when intracutaneously injected into rabbits and against which neutralizing antitoxic substances can be developed.

It seems quite likely that we may have been too academic in our established classifications of bacteria into toxin-formers and non-toxin-formers. The difference between the various species of bacteria in regard to toxin formation may be a quantitative one in which the potency of the toxin produced is in inverse ratio to the invasiveness of the microorganism. Thus, toxins are most highly developed in such bacteria as diphtheria, tetanus and botulinus bacilli, which do not actually invade the body but are saprophytically limited either to dead tissue or to mucous surfaces; while with organisms like streptococci and others which invade the body extensively, toxic substances of far less potency are required for the production of a profound toxemia. We have learned from the scarlet fever investigations, incidentally, that toxicity for man may occur without in any way implying toxicity for the ordinary laboratory animals, and that even within the same species, toxic action may be selective for individual tissues. Moreover, we have learned that neutralizing antitoxic substances can be formed against bacterial products which are heat stable and in many other respects differ from what we have hitherto called the "classical" exo-toxins. While these are the chief lessons we have learned from the scarlet fever investigations, they have also taught us that in approaching immunological investigation of any disease we must pay more attention to the clinical observation of the condition in man from which clues for investigation can often be deduced which cannot be obtained by any amount of animal experimentation.

It is from this point of view that I wish briefly to discuss the pneumonia problem.

III.

THE PNEUMONIA PROBLEM

Pneumonia has been the objective of attempted serum therapy since 1881 when the Klemperers treated cases with immune rabbit serum. Washbourn used immune horse serum as early as 1897, and other attempts followed with results as variable and fluctuating as the lack of preliminary knowledge would lead one to expect. The modern era of pneumococcus investigation was initiated in 1909, when Neufeld recognized the existence of serological types of pneumococci and advocated homologous type serum and the intravenous use of considerable doses. He also introduced the titration of such sera by its protective powers in mice and rabbits, and thus carried the problem to the point where—with some elaboration—it has remained since then. Therapeutic investigation followed in the clinics of Germany, and it is interesting to note that in summarizing results and prospects in 1912, Neufeld made a statement which is applicable, with slight changes, to the conditions as they exist today. Admitting that no final judgment could be rendered at the time of writing, that is, 1912, he wrote the following statement: ". . . efforts should concentrate upon the intravenous administration of highly potent sera . . . injected at early stages of the disease; observation in practice as well as theoretical considerations incline us to expect less effect upon the local process than upon the general systemic condition." He discouraged the use of serum, for the time being, except in cases in which the homologous relationship between the type of responsible organism and the serum could be controlled. Since that time, the principles of Neufeld have been elaborated and perfected and methods very much as he recommended them made available for clinical experiment, largely by the efforts of Cole and his assistants, and after ten years of experience we stand about where Neufeld stood in 1912, at least as far as our general confidence in the specific therapy of pneumonia is concerned.

I do not wish to imply that the work of Cole and his associates has been futile. Much has been learned and something gained in a positive direction, and this period of experimentation has been absolutely necessary for the development of the subject.

A fair estimate of the present situation can be obtained by citing a few of the more carefully prepared studies of recent years, such as those of Bloomfield and of Locke. Locke has taken account of the many variable factors that complicate the clinical experiment, and has reviewed the reliable evidence of others, besides considering a series of his own observation. His conclusions, written eleven years after Neufeld's summary, are astonishingly similar to

them. He gives, as we all must, considerable weight to the published results of Cole, but, in summarizing other observations, finds that the results as a whole, measured by final mortality rates, are but little better than those found in untreated Type I pneumonias. Locke, as Neufeld did, emphasizes the importance of treatment within the first three days, and expresses the belief that if it were possible to study enough cases treated within the first three days, the results of serum therapy would probably be considerably superior to those now available. Bloomfield is a little more optimistic, and although he admits that after the infection has progressed beyond a certain point no amount of serum will save, he thinks that the criterion of its usefulness is not so much the day of the disease as the presence and seriousness of the bacteremia.

The need for an improvement in the serum therapy of pneumonia has expressed itself in attempted modifications, such as the antibody solutions of Huntoon and the concentration method of Felton. Neither of these methods represents a departure from the original principles either of Neufeld or of Cole. Felton's method of globulin precipitation with distilled water is an excellent and simple technique for the considerable concentration of the significant antibodies in a smaller volume and with less serum protein. It should render possible the injection of larger antibody quantities with a diminution of serum sickness effects and in this way perhaps serve a useful purpose. Huntoon's dissociated antibodies similarly reduce the foreign protein contents, but as a result of the method of production, contain in addition to small amounts of serum protein a certain amount of bacterial antigen as a consequence of which these solutions produce strong non-specific reactions which may have a certain amount of therapeutic value. But it would appear from the extensive studies of Cecil and Larson, as well as of Conner, that no essentially new note has been struck by these substances, except this non-specific effect, which perhaps accounts for the occasionally beneficial results obtained by Conner in Type IV pneumonias and in streptococcus viridans cases, in spite of the absence of specific antibodies for these organisms in the solutions.

Essentially all these methods depend upon antibacterial substances, and it is not impossible of course that this type of serum may represent the best that we can do in this disease, in which case our efforts must be exerted in the direction of elaboration of the present procedure, with particular attention to early treatment.

It must not be forgotten, however, that while partial success is claimed with pneumococcus sera in the Type I cases, no one, including Cole, has at any time seen measurable therapeutic effects in Type II and Type III cases, an indica-

tion that, if there is a solution for the therapeutic problem in pneumonia, the antibacterial sera have not yet found it. It is the task of the immunologist, therefore, to reexamine the circumstances attending pneumococcus infection of the human being in search of other methods of approach, and in this the most logical step is to inquire into the mechanism by which the pneumonia patient often cures himself in what is perhaps the most dramatic clinical occurrence of infection—the pneumonic crisis.

Let us consider, therefore, whether there are any available facts regarding the spontaneous cure of pneumonia in man which may be utilized as clues for experimental reasoning.

Virulent pneumococci are neither agglutinated nor phagocytized in the average normal human serum; and the work of a considerable number of investigators who have studied this question (Neufeld, Gargano and Fattore, Lister, Chickerling, Dochez and Avery, Clough) is in general agreement that the antibacterial antibodies, while they appear in the course of recovery, are not present to any noticeable degree until just before, at the time of, or shortly after the crisis—and then never to a concentration which cannot probably be exceeded to a considerable extent in all cases in which energetic intravenous treatment with potent homologous serum has been instituted. Indeed, our knowledge of the time required for antibody formation would preclude the expectation of any powerful specific response of this nature within the period occupied by the average acute pneumonia.

The coincidence of the appearance of antibodies with the crisis, however weak, suggests the possibility of causal association between the two phenomena. But, although we know that, both in animals and in man, even moderate amounts of serum produce prompt disappearance of the organisms from the blood, this effect is accompanied neither by crisis nor by noticeable effects on the lesion. And this is true not only in human pneumonia but also in rabbits in which focal lesions of pneumococci have been produced by intracutaneous inoculation or by injections of infected agar. In consequence, we are forced to conclude either that the antibacterial antibodies do not represent the entire mechanism of recovery, or that the injected serum substances, though cleaning up the circulation, are not adequately capable of reaching the lesion itself.

The latter supposition is one that is plausible, for we have much experimental evidence that bacteria nested in tissues and inflammatory foci are to some extent entrenched against serum effects. Moreover, Kline and Winternitz, and again Lord, have emphasized the fact that pneumococci foci are—as Lord puts it—"partially isolated" from the circulation.

Thus, the incompleteness of the results obtained in the serum treatment of pneumonia

might be attributed to anatomic obstacles which prevent the circulating antibodies from reaching the lesion itself, rather than to any specific ineffectiveness of the injected antibodies. If this should turn out to be the case, the only hope for ultimate therapeutic success would lie in the earlier injection of polyvalent sera as soon as typical onset, etc. indicated the probability of pneumonia and before the establishment of consolidation. Whether this would be clinically feasible is doubtful.

It is still, however, a question of no little uncertainty whether or not the development of antibodies of the protective type represents the entire or even the essential mechanism of cure in pneumonia. Pertinent information has been obtained by lung puncture at different stages of the disease (Patella, Tchistovitch, Rosenow, Thomas and Parker). There is essential agreement on the following points: The organisms usually diminish in the lung early in the disease in favorable cases—but show no such diminution in the fatal ones. Occasional negative punctures, which indicate intrapulmonary destruction of the organisms, may be obtained several days before the crisis—in Thomas and Parker's series one four days, two three days, and six two days before the crisis; while in other cases organisms may still be present for twenty-four or more hours after the crisis. These observations suggest that bactericidal processes do not represent the entire mechanism of cure and that other factors, local or general, are at work.

Various suggestions have been made to account for the destruction of the bacteria and the development of the crisis without the consideration of antibodies. Jobling, Peterson and Eggstein determined that, at the time of crisis, there is a decrease in serum anti-ferments and an increased mobilization of the non-specific protease in the serum. They associate the crisis with the beginning of active autolysis, depending on altered relations between ferment and anti-ferment balance, and consider the fibrin and leucocytic débris in the lung as a potential source of toxic substances. Lord's point of view is essentially similar, except that the mechanism of dissolution, as conceived by him, depends upon a change in the hydrogen-ion concentration within the partially isolated lung and the establishment of an acid reaction which at first favours increased enzyme action and finally reaches the death point of the pneumococcus, when crisis and recovery follow. These views are interesting and, since they are based on experimental observation, cannot be ignored. However, they leave a considerable number of questions unanswered which must be taken into consideration when pneumonia is immunologically analyzed.

No one who has observed cases can question for a moment that in pneumonia there is a very potent toxemic factor. The sudden onset of the

condition, the high temperature, leuco-cytosis, the nervous symptoms developing long before extensive anatomical changes take place cannot be explained except by the absorption of toxic substance. The abrupt change at crisis which, in short time, may transform the clinical picture from that of profound toxemia to one of exhausted but safe convalescence, is much more in keeping with a conception of rapid neutralization of a poison than of any processes known to us due to enzyme action. Such processes are usually gradual ones. It is, however, conceivable that there might be a gradual development of a poison-neutralizing factor which, at the time of crisis, reaches that threshold of effectiveness which is quantitatively crossed within a relatively short time, and the crisis suggests nothing so much as an abrupt cessation of a poisoning. Moreover, as Thomas and Parker point out, microscopic necroses of the liver, suprarenal bodies, pancreas and kidneys may occur in lobar pneumonia which are not associated with the local presence of organisms and are in many respects analogous to similar lesions produced by diphtheria toxins.

Clinical evidence of a toxic factor in the symptomatology of pneumonia is so obvious that early investigators gave much attention to the search for poisonous substances in pneumococcus cultures. But, in spite of extensive efforts (Klempener, Isaeff, Kruse, Pausini, MacFadyen, Wadsworth and others), none of the materials obtained from culture filtrates or bacterial extracts exerted anything more than a limited toxicity in relatively large amounts. Similar failure attended all studies carried out with modifications of the simpler, earlier methods. Cole recognized a hemotoxin or methemoglobin-forming substance which has since been extensively analyzed by Neill and Avery, but, for the present, cannot be accepted as representing the true toxic element in pneumonia.

In spite of the relative feebleness of toxic substances for laboratory animals, however, attempts have been made from the beginning to develop antitoxic—as distinguished from antibacterial—substances by the immunization of animals. This was the idea of the Klempeners, and Wadsworth cites early work of Mosney and of Tizzoni and Panichi, who sponsored the same idea. Wadsworth himself believed that he had been able to distinguish between the antitoxic effects of sera produced with culture filtrates and the antibacterial action of those produced by immunization with whole bacteria, and suggested as giving him his best results the immunization with whole cultures of virulent organisms, as combining the two effects. Although, therefore, this phase of the subject is still in a purely speculative state, we have the unquestionable evidence of toxemia in the patient and some suggestions of antitoxic effects in certain immune sera. We lack definite evidence of a toxin, but

this circumstance we must reconsider in view of the recent developments with streptococci and staphylococci. We had no determinable poisons in these organisms until recently—at least, not by the classical experimental methods of earlier test. But we have learned from the work of the Diecks that there may be toxic substances which have no great potency for any laboratory animals and still may show toxic effects in man,—whatever the mechanism of such toxicity may be,—which may differ in heat stability, etc., from the classical exo-toxins and which yet may be neutralized by sera of animals produced either by the direct injection of these substances or by some method in which the total products are rendered effective within the animal, a modification of Dochez, or the injection of whole virulent cultures. From the work of J. T. Parker we know that some staphylococci will produce a toxin effective in rabbits only when intracutaneously administered and will produce antitoxic bodies only after intracutaneous immunization. We have learned, in other words, that organisms not too far removed biologically from the pneumococcus, may produce poisons which differ from the classical toxins we have been seeking for but are still effective in the essential therapeutic property of inducing the formation of neutralizing substances. Moreover, this work indicates that poisons innocuous for most animals may be potent for man, and that great potency may not be a necessary criterion for the ability of such poisons to produce antitoxins. Again, we have learned that invasiveness and toxicity may not run parallel, as in the case of our rats, killed by Dick streptococci with relative non-susceptibility to the poison.

Thus, if I have fulfilled my purpose, I have shown you that, through a prolonged and elaborate period of experimental and clinical observations, we arrive at the fork of two perfectly well marked alternative paths. If the cure of pneumonia depends purely upon antibacterial processes, the best we can do will be to carry to their logical extremes the plans at present followed, by methods of serum production which yield antibacterial substances, the concentration of these by various techniques and clinical efforts toward earlier administration. On the other hand, we may base some hope on the possibility of the development of an antitoxic principle.

It requires no great degree of originality to think of re-investigating the pneumonia problem from this point of view. This we are doing, and it is so obvious an effort that if many others are not doing it already, they will probably be doing it before long. At the Harvard Laboratory the plan that is being followed in an attempt to experimentally apply the reasoning that I have outlined consists in properly controlled studies of the toxic action of various pneumococcus preparations upon intracutaneous injection into man, relation of such toxic action to any possi-

ble neutralizing action on convalescent blood and, with the collaboration and assistance of Dr. White at the State Antitoxin Laboratory, attempts to modify the immunization of horses with pneumococcus products in such a way that, if a toxic principle can be obtained, our methods may disclose it.

IV

THE IMMUNITY PROBLEM IN TUBERCULOSIS

This is entirely too large a subject to be exhaustively covered in the time at our disposal, and I undertake it only in order to complete the discussion of the various types of immunological problems which concern us. The bare details of our knowledge can be briefly stated: Active immunization of man has so far been completely unsuccessful. However, we know that animals or man who are infected with tuberculosis are relatively insusceptible to super-infection, an observation made by Koch himself early in the history of experimental tuberculosis. Thus, if a tuberculous and a normal guinea pig are simultaneously inoculated upon the skin with like doses of living tubercle bacilli, they will differ during the first two weeks in that the tuberculous guinea pig, after a severe inflammatory reaction, will manifest a tendency toward limitation and healing of the new process quite in contrast to the steady progress of the lesion on the animal that was inoculated for the first time. Later, of course, when the tuberculous processes in both pigs are generalized, this difference between the local lesions will diminish. However we may investigate the subject, the basic fact remains that no increased tuberculosis resistance is conferred without the existence of a tuberculous focus in the body. In other words, the factor which lends a relatively high resistance to tuberculosis upon members of civilized and crowded communities is probably the acquisition of a mild tuberculous infection in early youth. It is, of course, true that, in the course of centuries, there probably has been a certain amount of natural selection which renders us as a race somewhat more resistant than are aboriginal races, but this racial resistance is not a very high one and the thing which protects most human adults from the average and probably frequent contact with tubercle bacilli is the fact that they are already in a mild and arrested form tuberculous.

It is true that antibodies can be produced in animals by proper treatment with tubercle bacilli, but passive immunization with such immune sera has been utterly ineffectual and antibacterial substances of this kind probably play but a minor rôle in the defense against this infection.

It is our opinion that the clue to immunity in tuberculosis is given by the mechanism of the tuberculin reaction. It is well known to you that tuberculous individuals and tuberous

animals become excessively hypersensitive to contact with the various forms of tuberculin. Such allergy can be produced in animals experimentally only by injecting either living tubercle bacilli or—as we have been able to show with Petroff—by the injection of dead, whole tubercle bacilli. Treatment with dissolved materials derived from tubercle bacilli or cultures do not induce such hypersusceptibility, and, though such treatment may develop antibodies of the usual varieties, it is not effective for the active immunization of the animals. The allergic or hypersusceptible state which, according to recent studies made by us with Ward and Jennings, is to some extent parallel with increased resistance, can be induced in guinea pigs only by the injection of bacilli—dead or alive—which are capable of producing tuberculous foci. Without a tubercle there is no tuberculin reaction and, in our opinion, without a tubercle there is no increased resistance.

A study of the immunological conditions as well as an original analysis of the occurrences in tuberculous infections seem to make it quite plain that local cellular processes are of paramount importance in the prevention of spread and the eventual destruction of the invading bacteria. In studying the phenomena of the tuberculin reaction in the course of the last four years, we have convinced ourselves that the true so-called "antibodies" have no relationship whatever to the development of tuberculin hypersusceptibility, but we have been able to convey tuberculin hypersusceptibility passively by injecting normal guinea pigs with extracts of the tuberculous tissue around lesions. Very recently, with Tamia, we have had some success in producing allergic reactions in normal guinea pigs by the injection of tuberculin which has been incubated with such tissue extracts, while similar incubation with serum containing antibodies for the tubercle bacillus has no such effects. Our own observations as well as the careful study of the extensive literature led us to suspect that the essential mechanism of resistance to the tubercle bacillus should be sought in the activities of the cells that constitute the specific inflammatory reaction known as the "tubercle," perhaps in the formation of a substance of an enzyme-like nature, certainly not identical with the ordinary antibodies, which are also formed, but probably play a secondary rôle. It is more than likely that the insolubility which is conferred upon the tubercle bacilli by their waxy and lipoidal constituents has necessitated the development of a mechanism basically different from that which underlies resistance to other bacteria, and it may well be that the tissue mechanism around the tubercles is that part of the story which concerns protection against the bacilli in their acid fast condition. The true antibodies may still play a minor rôle in the total mechanism, both by direct action and phagocytosis.

enhancing properties exerted towards the non-acid fast individuals.

Fortunately for the human race, the tuberculosis problem is being energetically attacked by sanitary and hygienic campaigns, and attention to nutrition, and personal and community life is already being attended by astonishing success. Moreover, a great deal of work is being done along lines of chemotherapy, the most recent efforts being those reported from Copenhagen where Mollgaard, using samocrysinsulphur gold salts, sodium aurothiosulphate ($\text{Au}(\text{S}_2\text{O}_3)_2\text{Na}_2$), together with a serum which is supposed to neutralize the toxic effects caused by the gold preparation alone, claims to have arrested experimental tuberculosis in calves, guinea pigs and monkeys. So far, this treatment is entirely in the experimental stage, and the published results do not deduce sufficient evidence to persuade us to believe that the therapeutic problem has been solved. Certainly chemotherapeutic efforts have not sufficiently progressed to permit us to discontinue investigations along purely immunological lines.

V.

THE PROBLEM OF IMMUNITY IN SYPHILIS

In syphilis we have a problem that is immunologically closer to protozoan infections than to the bacterial ones. There is an enormous literature on the immunological observations of the disease in human beings, and since 1903—when animal transmission became possible,—much that was learned in man has been confirmed in animals. Briefly, the principles of immunity in syphilis are as follows:

- (1) The syphilitic subject acquires definite resistance to re-inoculation soon after the appearance of the primary sore; in other words, as soon as the virus has become generalized.
- (2) This resistance, high though not absolute, persists throughout the secondary and into the tertiary stage, probably declining somewhat in the tertiary periods.
- (3) When syphilis is entirely cured, both human and animal observations indicate a complete return to susceptibility to re-inoculation; in other words, resistance remains only so long as organisms are still present in the body. In this respect there are many analogies in the protozoan diseases, particularly in trypanosomiasis in cattle and probably malaria.

We say with the confidence of several years of experimentation on rabbits that no method of active or passive immunization in man has been developed or has even yielded any hope of success in spite of extensive and frequent claims. The organism, which can be actually cultivated as *treponema pallidum*, as soon as it has been grown, no longer possesses any of

the biological characteristics of the virulent organisms which we see in the lesions by dark-field, except a superficial morphological similarity. It can be injected into rabbits in enormous amount and produces agglutinating and other antibodies. The rabbits, however, are never infected by it, nor are they immunized by any amount of such treatment against inoculation with the virulent organisms. The serum of syphilitics, in spite of some contrary claims, does not exert any antibody action upon the culture treponemata, and antigen made with these organisms has no value for Wassermann reactions. The Wassermann reaction depends, incidentally, upon a mechanism that has no relationship to true antibodies, and there remains of specific relationships between the cultivated *treponema pallidum* and syphilis nothing except the Luetin reaction, which has not fulfilled the expectations with which it was at first received.

In syphilis, immunity of the tissues seems to be quite definitely associated with actual reaction to the living virulent microorganisms. In a large series of experiments extending over a number of years, in which, with Hopkins, we studied these relations in rabbits, we could find no other means of immunizing except with the living organisms, the only evidence of immunity being that a testis which had completely recovered from an experimental syphilitic lesion within several months could not be re-inoculated, although the opposite testis was susceptible even during the time when its mate still harboured an actual lesion.

Fortunately, the hopeless situation for theoretical immunization and vaccination which these facts indicate has been offset by the brilliant success of chemotherapy, and it is better to know the facts, though discouraging for the time being, than to have a lot of false confidence in misleading observations.

VI.

IMMUNITY IN FILTRABLE VIRUS INFECTION

In the filtrable virus infections, our knowledge of immunity is hardly more than rudimentary, but the little that has been learned is sufficient to indicate that, in diseases of this nature we are confronted with problems materially different from those existing in bacterial infections. In the diseases in which it has been possible to make reliable observations such as,—for instance,—smallpox, poliomyelitis, foot and mouth disease, hog cholera,—one attack appears to confer immunity, and in these conditions, as well as in rabies and herpes, active immunization can be accomplished, but only with a living, never with a dead virus. Dead virus appears to be useless. Even when fully virulent material is injected into animals and for some fortuitous reason fails to infect, the animal remains susceptible to subsequent inocula-

tion. This has been repeatedly noted in monkeys in connection with poliomyelitis.

There does not seem to be any hope, therefore, of developing methods of vaccination with dead infectious materials analogous to those practicable in some bacterial diseases like typhoid fever. Immunity occurs only when living virus and tissues have reacted. Just what this means it is not possible to say with any certainty, but it is our opinion that this may depend upon the fact that, in causing disease, most of these viruses penetrate into the interior of the tissue cells. Both the injury and, in consequence, the mechanism of immunization are intracellular processes and the virus must be alive in order to penetrate into cells where it does its injury and, if the cell survives, sets in motion the reaction of resistance.

Active artificial immunization is feasible, therefore, only in cases in which attenuation of the virus can be carried out, either by passage through animals of another species (smallpox, rabies), by the addition of chemicals, by drying, by partial initial neutralization with the serum of immune or hyperimmune animals, or by high dilution—all of them methods which imply the production of a mild form of the actual disease in the subject to be immunized.

In many of these diseases the serum of convalescent or of successfully vaccinated subjects develops substances which possess demonstrable viricidal powers. In other words, mixture of the serum of such animals with the infectious material and incubation for an hour or longer before inoculation renders the virus innocuous. This has been shown for smallpox virus within 9 to 14 days after the vaccination of calves, and is probably the reason why the children born of mothers who have recovered from smallpox during gestation are temporarily immune. It is true of foot and mouth disease, of rabies and of poliomyelitis. It has also been claimed and is probably true of herpes in rabbits, though experimental reports in this case are still somewhat contradictory and we ourselves have not yet been able thus to neutralize the strain of herpetic virus with which we are working. As a result of such observations, attempts have been made to employ the sera of convalescents and of vaccinated subjects for therapeutic purposes; but though the principle is a sound one, and although temporary passive prophylactic protection may be achieved in this way (foot and mouth disease, rabies), the treatment of active infections with such viricidal sera has been, on the whole, disappointing. In poliomyelitis only has there been a certain amount of encouragement—but even in this case the results have been inconclusive. Here again the difficulty may be in the intracellular localization of the virus during the active stages of the disease—a circumstance which would protect it from contact with any agent, however potent, injected into the circulation.

A considerable number of filtrable viruses are now conveniently available for experimental study and there is a fair prospect of our gaining a clearer understanding of their biological properties, though, of course, as Flexner points out, our inability to see or to cultivate these invaders should make us even more careful in drawing conclusions than in ordinary bacteriological work; rather than less so—as seems to have been the case in the earlier encephalitis studies.

We can perhaps best illustrate the nature of the difficulties encountered in the investigation of the filtrable virus infections by briefly discussing the problem of encephalitis lethargica. It will be remembered that, in 1919, Strauss, Herschfeld and Loewe reported that they had been able to infect rabbits with a virus obtained from cases of this disease. Shortly before this Grüter and, at about the same time, Löwenstein described the successful inoculation of rabbits with a filtrable infectious agent obtained from vesicles of febrile herpes. The results of Strauss and his collaborators were variously confirmed, and herpes inoculation of rabbits is so easily accomplished that no one who has attempted it seriously has failed. For a time it seemed quite likely that the etiological problems of encephalitis were well on the road toward solution, and the indistinguishable similarity—both symptomatically and pathologically—between the encephalitis and herpes rabbits suggested the probability of a close relationship between the two infectious agents. By most of the observers who claimed successful results in both cases, however, it was admitted that, while herpes infection of rabbits was easily accomplished and readily carried indefinitely from cornea to cornea or from brain to brain, the transfer of the encephalitis virus from man to rabbit and from rabbit to rabbit was more irregular and difficult. The material from human encephalitis cases used for transfer to rabbits by the earlier observers consisted to some extent of the nasal and pharyngeal washings of active cases. Such material is not above suspicion, especially in the light of the discovery of an infectious agent indistinguishable from herpetic virus in the saliva of normal individuals. This is an observation which was reported by Levaditi and has been several times made by us, both in normal people and in individuals suffering from acute colds, though Flexner states that he has not yet run into such a case. However, in addition to this, the early observers also reported successful transfer with brain substances obtained at autopsy and with spinal fluid. In spite of these apparently unequivocal results, later investigations did not, in every case, confirm them. Flexner and Amoss, in a large series, and we ourselves with F. Parker, Jr., in a smaller number of attempts in which the brain substance and spinal fluids of encephalitis cases were used, failed to obtain a single successful rabbit transfer—not one of the inoculated animals developing anything resem-

bling either the described conditions or the herpetic disease. Flexner, in a recent series of papers, frankly suggests that the etiological problem of lethargic encephalitis is probably unsolved and that the results reported by earlier investigators may perhaps have been due to confusion with a herpetic virus.

The entire question of the nature of the encephalitis virus and its relationship to herpes is, therefore, in some confusion, owing to what seem to be direct contradictions of experimental results. As we have stated before, successful transfer of encephalitis was reported by Strauss and his collaborators, was confirmed by Thalheimer and then by McIntosh and Turnbull, who, after a large number of negative attempts, succeeded in obtaining a few passive transfers from man to monkeys and, later, from the monkey to rabbits. Levaditi and Harvier, Kling and Doerr and Schnabel, to mention only the most prominent workers in this field, all of them reported successful transfers—obtained, to be sure, with more or less difficulty, but—nevertheless—definite when obtained. The last named investigators were the first to suggest the relationship between the encephalitis and the herpes virus; and they attempted to prove identity by cross immunization. In direct opposition to these claims are the negative results of Flexner, as well as our own, and since it is never wise to assume that differences of result can be explained by error on the part of other investigators, especially when those who report contradictory results are men as experienced as Levaditi, Doerr and their associates, we must try to seek an explanation on reasonable grounds, the very fact of experimental discrepancy perhaps revealing an important principle.

There would seem to be only two possible explanations that could harmonize the contradictory results. One of these, suggested by F. Parker, Jr., favoured by Flexner and actually taken into consideration by Doerr and Schnabel in one of their investigations, is the possibility that herpes virus may often penetrate into the circulation and thence to other parts of the body, and when this happens to occur in cases that are at the same time suffering from encephalitis, the herpes virus would be transferred to the experimental animal with the spinal fluid and brain, representing a purely fortuitous contaminating infectious agent. Bastai, indeed, reported the finding of herpes virus in the spinal fluid of a number of cases that had extensive herpes but without having at any time suffered encephalitis. Doerr and Schnabel, who do not favour this view, failed to confirm Bastai's observations in 16 attempts of similar transfer from non-encephalitic cases. Flexner's recently reported case of a typical herpes virus derived from the spinal fluid of an individual suffering from tertiary lues seems to furnish at least one absolutely authentic instance of such deep penetration of the herpes virus in a non-encephalitic in-

dividual. This explanation, strange as it may appear, has, therefore, some basis in observation.

There is only one other possibility that we can see at the present time as accounting for the experimental discrepancies without the assumption of this ubiquitousness of the herpes virus, namely, the possibility that our own complete failures and those of Flexner, as well as the difficulty of transfer encountered by most European observers are due to an attenuation for rabbits which takes place in the herpes virus after prolonged sojourn in the human nervous system. There is sufficient analogy for such a train of thought in the class of filtrable viruses, the most well known instances being the attenuation of smallpox virus for man by passage through cattle and the almost complete attenuation of rabies for man by passage through rabbits. The thought has come to us, largely as a consequence of studies with herpes virus which we have been making for several years and which are being continued at the Harvard Laboratories at the present time by Breinl.

In studying the viricidal properties of the sera of actively immunized rabbits, we have been seeking a method of more exact dosage. The technique developed for this purpose by Dr. Breinl consists in making emulsions of the total brain mass of rabbits that have died of the infections and injecting (intracerebrally) dilutions of such suspensions, ranging from one to one thousand to one to one million. The injection or dilutions down to one to one thousand killed the rabbits with typical symptoms, with regularity and without diminution of the incubation time. When, however, the dilutions reach or exceed one to one hundred thousand, the disease may be prolonged, and—occasionally—animals will survive after a brief febrile period. On several occasions when Dr. Breinl re-inoculated animals which had survived the smaller doses, instead of being totally immune, as are rabbits that have survived severe corneal infections, these animals, though showing no symptoms until many days after the controls had died,—in one case 32 days—eventually developed a subacute condition of lethargy and coma not unlike the human disease, in which they remained for 3 or 4 days before they finally succumbed. The clinical courses in these animals had little resemblance to the usual picture of acute herpetic encephalitis and appeared to indicate that an increased degree of resistance, or partial though incomplete immunity could convert the rabbit disease into one quite obviously suggesting the human.

The upshot of the matter is that it is impossible at the present time to decide whether or not there is any relationship between encephalitis lethargica and herpes, though the preponderance of evidence would seem to us against an identification of the two. Yet we believe that by the possibility of experimentally modifying both the virulence of the infectious

agent and the susceptibility of animals much further information can be obtained. Until this and other methods have been pursued to a much more thorough and critical degree, we must—with Flexner—regard the etiological problem of encephalitis as unsolved.

In endeavouring to give you a survey of some of the problems with which the immunologist is struggling, it is more than likely that I have failed in many particulars, both in sufficient qualification of broad generalizations and in clearness of the details that the limited time has permitted me to discuss. In spite of foreseeing this possibility, however, I chose to cover as broad a field as possible in order that I might convince you of the intimacy with which the problems that we are studying touch upon those of medical practice; to illustrate to you how

manifold may be the reactions by which the body defends itself against the invasion of other forms of life; to impress upon you how necessary is the comprehension of these processes for a rational clinical understanding of infection and for the development of therapy.

I shall count myself fortunate if I have conveyed to you to some slight degree the essential simplicity of immunological conceptions and the value that our methods of approach may have for a closer cooperation between clinic and laboratory. Let us not forget that many of the clues by which knowledge of immunity has often been initiated have been furnished by the observations of scholarly physicians at the bedside. And let us hope that by conferences such as this one the physician may be encouraged to submit his clinical problems to the immunologist more frequently than this has been the practice in the past.

ORIGINAL ARTICLES

CANCER AND THE SUN

BY FREDERICK BRYANT, M.D., WORCESTER, MASS.

CANCER is the great outstanding, unsolved medical problem,—the most unfortunate and lamentable therapeutic failure of our generation. Of all diseases it most challenges modern science. It has become the despair of the investigators for a definite cause and a specific cure have vanished at every approach, and the arch enemy of the race, the greatest human tormentor, “still sits grimly in his stronghold.” Nevertheless, there is now in our possession, as the result of the accumulation of cancer knowledge, certain facts and well founded beliefs, from the critical study of which we may determine our possibilities of escape, relief or cure.

CANCER—CIVILIZATION

I shall call your attention to one of these conclusions which I believe offers the best vantage ground in cancer control and the most promising avenue of escape. This includes the following facts and beliefs: that cancer is a disease of civilization; that primitive races are practically immune; that certain irritations such as the Roentgen ray, Kangri basket, betel nut and some occupations excite cancer; that it is highly probable that there exist, in the subtle complex of food and habits of modern life, many other cancer irritants which we cannot as yet clearly demonstrate; and that civilized man seems to have cursed himself with cancer exciting evils of his own creation.

CANCER—J. ELLIS BARKER

Having held the view for some time that cancer finds multiple exciting causes in civilized

life and customs, I have been decidedly impressed by a recent remarkable publication. While in London last summer I desired to gain the twentieth century opinion of that ancient and learned medical centre, regarding cancer. My attention was called, for it was the talk of the medical men of London, to a book published in June. So great was the demand for this book, both by the profession and the laity, that the edition was immediately exhausted and it was reprinted the following month. The author is J. Ellis Barker and it bears the startling title, “Cancer—How it is caused—How it can be prevented.” It is dedicated, “To all those Men and Women who do not wish to die of Cancer.” It is introduced and sponsored by Sir W. A. Lane. It represents an enormous amount of labor, for Barker, like Hoffman, has evidently searched the ends of the earth for cancer information. It is unquestionably the best popular treatise on cancer ever written.

CANCER—FOOD

Barker appears to be the first to recognize and express in a definite way that civilized man is incurring a large cancer exciting possibility in the manner in which he preserves and prepares his food. He considers this a chronic irritative poisoning. At the same time the vitamin content of the food suffers a loss or is destroyed altogether. These vitamins render the tissues resistant and impart to them both health and vigor. In this poisoning time is a long element. Many years are necessary for its full enactment. This cancer prodrome

is a matter of decades. This coincides with the fact that cancer is a disease of advanced years. Here is revealed a tremendous source of weakened resistance. These vitamins are an absolute essential to a well balanced food. They can only be obtained in satisfactory and safe abundance in fresh cell life either animal or vegetable. Upon such the savage man existed. On the contrary civilized man partakes of very little if any absolutely fresh food. His animal food is made tender by decomposition and is exposed a long time to refrigeration. The vegetables which he consumes are far from fresh due to his city dwelling. Much of this food is over cooked under extreme heat pressure and the vitamins as well as the mineral salts make their escape in the boiling water. His bread, "the staff of life," is for the most part completely devitamined. His milk, the one perfect food when fresh, follows the same pernicious vitamin destruction to arrest its decomposition over miles of transportation. Food deprived of its vitamins weakens the bodily defense. The absorption of the chemical preservatives, although exceedingly small in quantity and covering a long period of time, acts as a chronic irritative poisoning to the alimentary canal.

Barker is not the only prophet who is warning civilized man to look to his food. Cancer student in various parts of the world are eagerly scrutinizing the relation of food to cancer. Hoffman from his most extensive study concludes that diet is a probable causative factor. Dr. William Mayo believes that there is something in the habits of civilized man in the cooking or other preparation of his food which acts to produce a pre-cancerous lesion. Dr. Percy Howe's epoch making research on nutrition and tooth decay wherein he establishes the fact that necrosis of the teeth comes from within or from faulty nutrition adds another powerful testimony to Barker's argument that the absence of vitamins in food lets down the bars of body defense. From various authoritative sources, therefore, comes the common belief, that there is something decidedly wrong with civilized man's food and that it is in some way responsible for the great cancer increase. From this conclusion it would seem possible for civilized man to escape this disease curse by returning to more primitive ways of living.

CANCER—CONSTIPATION

Barker has much to say about the evils of constipation. Here again we note a decided contrast between the wild and the civilized man. "Apparently civilization and constipation go hand in hand." Constipation and cancer are practically unknown to the savage. They both infest civilization. Is there any col-

lusion between them? Recent writers believe there is. Some would make it a chief causative agent. The fact that one-third of all cancers are in and about the food canal is significant. Long continued constipation is believed to lead to chronic poisoning of the system from auto-intoxication and absorption. The general resistance is hereby weakened and the local irritative effects of hard dried movements file and gauge the delicate linings of the bowels. The habitual employment of purgatives tends to aid the pernicious program of irritation.

CANCER—THE SUN

I believe that Barker should have included the sun in his argumentative comparison between modern and primitive living in cancer prevention. My purpose in this writing is to express my full belief in the sun as a help in the prevention and cure of cancer. I offer this as the only justification of reopening this time-worn and well-nigh useless cancer discussion. The savage exposed himself directly to this protective agency and verified the truth that he who goes naked has no cancer.

It has long been known that vegetable life depends upon the sun in a vital way; it is likewise beginning to be believed that the human plant equally needs the sun for its best preservation and disease defense. In the childhood of the race mankind worshipped the sun. All forms of life love the sun; the plant bends its stalk and turns its leaf toward it and the infirm animal crawls out of his dark hole to comfort himself in its healing warmth.

Civilized man has shut out the sun at every turn and now suffers the sad results. He has thereby deprived himself of one of Nature's protections which has opened the door to the invasion of diseases, chief among which is cancer.

CANCER—RESISTANCE

Cancer is so unsparing of its victim and remedies are so unavailing that one is apt to be unmindful of Nature's attempt to resist the deadly invasion. As in other diseases so too in cancer Nature throws up her defense works. This fact must never be forgotten or lost sight of. Dr. McCarty, of the Mayo Clinic, has demonstrated at the periphery of a growing carcinoma there is a zone of hyaline and fibrous tissue changes and a leucocytosis, which gives evidence of Nature's attempted resistant encapsulation.

CANCER—UNHEALTHY TISSUES

The idea begins to prevail that cancer never develops in healthy tissues, but that it finds easy access to the tissues rendered unhealthy and non-resistant by the chronic irritative poisonings of civilization. That a lowered resistance of the tis-

sues precedes cancer, seems destined to common acceptance.

CANCER—TREATMENT

Is it possible for us to avoid cancer? The savage man escapes it. Let us take a lesson from him and modify our ways of living to a more natural and less artificial existence. Should we not seize upon this as the most strategic escape from our greatest disease enemy? If the exciting causes of cancer are to be found in our food or habits of life let us search diligently for them for by their apprehension and removal we have a most valuable preventive possibility and the solution of the cancer problem.

CANCER—BIOLOGIC LIVING

The logical conclusion of this whole argument for cancer prevention is a return to the "simple life" or biologic living. It calls for a less civilized food, balanced with fresh cell life, imparting the highest possible vitamin content. It means the creation of a new hygiene and a new prophylaxis against disease, by maintaining all tissues in a resistant, young and healthy condition. This biologic food reform rests upon the sound foundation of well-established facts. McCollum concludes from his most scholarly researches; that man must consume the essential constituents of a normal diet; that he must properly digest and absorb it; that in order to maintain vigor and the characteristics of youth he must promptly evacuate the undigested residue from the intestines before extensive absorption of the products of protein decomposition can take place and that such a diet must be made up mainly of milk, dairy products, the leafy vegetables, whole-wheat bread and fruits. Eat everything that is edible in a raw fresh state. Live out of doors and exercise with the body exposed as much as possible directly to the sun. Sleep on the porch, veranda or balcony. Live extensively from food from the garden of your own cultivation. In short, a return to more primitive, natural living is the great essential in the twentieth century program of cancer prevention.

But what shall we do when cancer comes? Of all that countless myriad of remedies which have been advocated, since time immemorial, only two have survived the crucial test of time—surgery and short wave-length radiation. The latter Dr. Frank Harvey has befittingly termed "the surgery of light." This new remedy does not attempt to displace but to aid, supplement and become the hand-maid of the old surgery. The intense study of the "surgery of light" has added much to our knowledge of the biology of cancer, and there is a hope that it will eventually work out the solution of cancer therapy. In almost every cancer field of operation these two remedies are used in a judicious union. This combination is giving a decidedly better outlook

in the treatment of this dread disease. So much confidence has been developed in this method that some authorities are boldly asserting that in most situations cancer can be cured if discovered early. Hoffman recently declared, "The evidence is overwhelming that cancer cases are being arrested or cured to an increasing extent and that many who might have died from cancer die from other diseases as a result of early operation or qualified treatment otherwise."

That the new surgery has definitely taken its place along with the old in the treatment of cancer is abundantly evidenced by the facts; that leading surgeons throughout the world are combining it with their operating in a routine way; and that the American College of Surgeons after a very thorough and conservative investigation of radium concluded in an official report, that its surgical value was established beyond dispute. In this connection, Dr. Ewing remarks, "The first rational treatment of cancer ever devised." Dr. Wilkins states, "Radium is one of the most valuable aids to surgery." Dr. Kennedy states, "Often a combination of radium and surgery gives better results than either means employed exclusively." Dr. Chase recently concluded, "We will employ all the various modalities of surgery, including with the knife and the cautery, those radio-active agents, the roentgen ray and radium, in the employment of which such great strides have been made within the last few years."

During the past summer I interviewed Mme. Curie, in Paris, Dr. Rollier, in the Swiss Alps, and Dr. Reyn, at the Finsen Institute, in Copenhagen, to determine the use they are making of radium, natural and artificial light in the treatment of disease, with the object of applying the latter as an adjunct to radium in the treatment of cancer.

In all probability there is no place in the world where radium is as scientifically prepared and as skillfully administered as in the Curie Foundation of the University of Paris. The radium products are made up by Mme. Curie, herself, and applied by Dr. Regard, an acknowledged radium therapist. I was impressed with their conservative methods in the employment of fractional rather than massive, lethal doses. With both radium and the roentgen ray smaller doses for longer periods prevailed, as opposed to larger doses for shorter periods. For instance I saw a small amount of radium removed from a growth which had been in place for five days. It has been demonstrated that short wave radiations destroy the chromatine of the nucleus of the rapidly dividing cell at the metaphase of mitosis. The prolonged or fractional dose gives the radiation an opportunity to destroy different crops of cells when they reach the sensitive stage in their life cycle. One dose however large only catches a certain number of the maturing cells while divided doses are bound to intercept all

the cells at times when the accomplishment of their destruction is possible. Fractional dosage, therefore, accomplishes most in destroying the growth and in stimulating rather than breaking down Nature's defenses.

From my observations of the "sun cure," in Switzerland where the sun is used at an elevation of five-thousand feet and the "sun lamp" or artificial production of the sun, at Copenhagen, my faith in the value of the sun was greatly enhanced and I became fully convinced of its health stimulating properties when admitted directly to the skin. The "Sun Doctor of the Alps" demonstrated to our entire satisfaction hundreds of debilitated, bed-ridden, flabby, emaciated, tubercular patients who had become robust and muscular without either massage or exercise treated only by the pure rays of the mountain sun. Finsen's "sun lamp" which reproduces the sun's spectrum in its entirety and also adds to its curative richness a variety of shorter wave lengths seems to accomplish equally gratifying results in a much shorter period of treatment. I firmly believe in the Rollier and Finsen methods combined, using the sun when possible and the "sun lamp" when it is not available. There are those who believe cancer to be a general disease with local manifestations like tuberculosis. If the sun will produce such astonishing cures in surgical tuberculosis why is it not logical to give it a tryout in cancer which has some points at least in common? No other agency equals the sun in building up individual resistance, in bringing the entire organism to a quick return to normal function. It lends hope, cheer and a determination to fight disease. I advise all my cancer patients to indulge in the sun when it is possible exposing not only the cancer area but the entire body directly, as a helpful accompaniment to the roentgen ray and radium. I expose the local lesion to the "sun lamp" until a chocolate-brown tanning is produced. Following such exposures much more roentgen ray intensity can be endured by the skin because of the protective tanning. In case of over dose the "sun lamp" accomplishes a neutralizing effect of value.

This combination of the sun and the shorter wave lengths clearly tends to assist Nature. Remembering McCarty's findings we note that the sun increases leucocytosis which elevates at once the resistance of the surrounding tissues. The roentgen ray and radium stimulate a definite connective tissue encapsulation while at the same time the vulnerable rapidly dividing cancer cells are destroyed.

In the treatment of cancer there is no place for the faddist who has or sees but one method whatever that may be. No one procedure has the right of way in every case of cancer. The most promising hope of the time is the radio-surgical combination, which is a wise unbiased selection of those methods which have given the

best results in both the old and the new surgery. The highest function of medicine is to assist Nature. A human being suffering from the "great black plague" is to be treated, not a cancer. The surgeon or the radiologist must not in destroying the cancer, destroy the patient also. The paramount question always is, what is best for the patient? Is there any possibility of cure from the wisest selection of remedies at our command? If not, what will give him the least suffering, mutilation and the longest period of comparatively comfortable existence? The clinician or family physician is the man of the hour. He is becoming better and better posted on the importance of detecting the early whisperings of malignant disease and as to its relief possibilities. He can be trusted to safeguard his patients' interests. He, therefore, wisely calls the surgeon and the radiologist into a group study of the case in question. In almost every hospital community this combination is possible. We enjoy, here in Milford, all the requisites for such study and treatment of cancer cases. It is a great convenience for the afflicted and reflects confidence and credit upon the home institution.

Finally, what we know and what we surmise about this ever increasing malady give us helpful clues as to possibilities of escape. A number of chronic irritative poisonings are the most probable exciting causes of cancer. They attain in civilized communities. The savage living in his wild rugged state knows no cancer. Him civilized man must study and in some ways strive to imitate. He must not exclude the sun from his body or the vitamins from his food. He must live a more natural life. He must remove every pre-cancerous irritation. He should make use of all cancer information that is published from responsible sources. If any suspicions arise as to cancer possibilities he should go at once to his physician, who will pass upon the evidence and if necessary will bring to his relief those agencies which are proving most effective in the twentieth century treatment of cancer.

THE INCREASE IN THE REGISTRATION AREA

THE registration area of United States for deaths has increased from 1880, when it was begun, in two states, District of Columbia and 19 cities, to 39 states, the District of Columbia and 18 cities in the unregistration area.

The birth registration area was first established in 1915 and includes 33 states and the District of Columbia, or 76 per cent of the population of the United States.—*Bulletin Conn. Dept. of Health.*

GASTRIC AND DUODENAL ULCER VARIOUSLY TREATED*

A Study of End Results

BY THEODORE C. GREENE, M.D., BOSTON

THE medical and surgical treatments of gastric and duodenal ulcers are essentially applied problems in the chemical and motor functions of the stomach. Since gastric hyperacidity is not always present in either kind of ulcer, and since greater care than is usually taken is necessary to determine whether the acidity is neutralized, medical treatment has been challenged as being often ineffective¹. On the other hand, the various forms of surgical treatment have been questioned². Such a discussion naturally leads one to examine the results that have actually been obtained.

Eggleston³ reports 156 cases treated medically, with 72% free from symptoms for at least three years, and Sippy⁴ gives a higher percentage of success. Joslin⁵ reports 131 gastric ulcers treated medically, with the following results: 39% well, 42% relieved, 12% unrelieved, and 7% dead, after a period of years.

Of the many surgical reports only three are included. C. H. Mayo⁶ reports 438 cases of duodenal ulcers that have been followed; 70% were well, 27% improved, and 3% unimproved. Of 59 cases treated by gastro-enterostomy, Pool and Dineen⁷ found 50 cases well after an average of three years. Scudder⁸ reports 99 out of 108 cases of gastric ulcer practically well after many years. Of 94 cases of duodenal ulcer, 88 were practically well after a varying number of years.

Taking the results reported in other papers, we find that complete or almost complete relief was obtained in 70% of 331 cases treated medically, and in 85% of 1019 cases treated surgically.

However, grouping statistics from different clinics is obviously misleading. In order to afford further evidence on this subject, a study has been made of the results of treatment at the Peter Bent Brigham Hospital, in those cases which were followed by letter, examination at the hospital, or reentry. In this report, cases treated medically are included only where a primary, unquestioned diagnosis of ulcer was made; and in all surgically-treated cases, an ulcer was demonstrated at operation.

CASES TREATED MEDICALLY, 1913-1922

Gastric Ulcers—24 Cases

	Years					Total
	1-1	1-1½	1½-2	2-4	4-	
Complete Relief	3	1	4	2		10
Partial Relief	2	1	1	1		5
No Relief	3	5		1		9

*From the Surgical Clinic of the Peter Bent Brigham Hospital.

Duodenal Ulcers—15 Cases

	Years				Total
	1-1	1-1½	1½-2	2-4	
Complete Relief	1	2			3
Partial Relief		6			6
No Relief	1	2	1	2	6

Of the medically-treated patients in this series who reported that no relief was obtained, nine came to operation. Five patients in whom gastric ulcers were diagnosed were later operated upon at this hospital. Four of these proved to have gastric ulcers, and the fifth had a duodenal ulcer. In another case perforation occurred within less than a year and a duodenal ulcer was seen at operation. In still another case, the patient experienced a haemorrhage after four years.

Three cases diagnosed as duodenal ulcer came to operation. One case was operated upon elsewhere. Of two patients operated upon here, one had a duodenal ulcer, and no lesion was found in the other, although definite stasis had been shown. Another patient suffered a haemorrhage after one year, and another died following perforation two months after leaving the hospital. This patient, the other patient with perforation, and several others had refused surgical treatment, which had been advised by both medical and surgical services.

CASES TREATED SURGICALLY, 1913-1921

Gastric Ulcers—40 Cases

	Years				Total
	1-1	1-1½	1½-2	2-4	
Complete Relief	1	1	10	20	34
Partial Relief		1	2	1	4
No Relief		1		1	2

Duodenal Ulcers—70 Cases

	Years				Total
	1-1	1-1½	1½-2	2-4	
Complete Relief		3	11	37	45
Partial Relief	2	1	8		11
No Relief	2		2		4

Multiple Ulcers—7 Cases

	Years				Total
	1-1	1-1½	1½-2	2-7	
Complete Relief		2	1	1	4
Partial Relief	1		1		2
Haemorrhage			1		1

In this series of 117 patients, who were treated by surgical methods, one suffered a haemorrhage after two years. Six patients in the series obtained no relief, and all underwent a second operation. Of these six, there are no reports of the results of the second operation upon two patients. The other four, reoperated upon at this hospital, obtained complete relief after the second operation; one reported after one year, and three after two years. Thus we

know that complete or partial relief was ultimately obtained by all the 117 patients except in the case of the other two, who also may have obtained relief.

SUMMARY

	Medical	Surgical
Complete Relief	13	93
Partial Relief	11	17
No Relief	11	6
Complications	4	1
Total	39	117

The complications occurring among the cases treated medically include two haemorrhages and two perforations, and one of these perforations proved fatal. Among the cases treated surgically there was one haemorrhage. In considering the cases treated surgically, the operative mortality must be remembered, for no patient who died from the operation would be included in this series of followed cases. With the operative mortality of approximately 2%, reported below, two or three patients in every 117 would probably die.

DISCUSSION

There is little doubt that in dealing with large numbers, surgery gives better results than medicine. Patients must, however, be dealt with as individuals, treating some medically and some surgically, according to the nature of the case. For this reason, it would be folly to argue from the above statistics in considering the treatment to be advised for the given patient. Consider, for instance, the cases which the medical service had to treat because surgical treatment was refused.

W. Mayo⁹ says that all agree that in the face of repeated haemorrhages, or of mechanical obstruction or deformity, surgery should be followed; in other cases, medical treatment is to be chosen. Bevan¹⁰ would want an ulcer of his own treated medically until haemorrhage, perforation, obstruction, or no relief followed. Sippy¹¹ states that medical treatment should be followed unless X-ray studies show that the ulcer is not being influenced. Crile¹² states that he would try medical treatment for ten to fourteen days, and then operate if there were no improvement. Naturally, no surgeon would operate during the initial bleeding of an early ulcer, and most surgeons agree that operation during active haemorrhage is injudicious.

If medical treatment were entirely free from danger, there would be no hesitation in following it first, even if it were seldom successful; thus the risk of an operation would be avoided, should the medical treatment prove successful. The weakness of medical treatment is that it may relieve without curing. Unless the patient can remain in the hospital longer than most patients can, the success of this treatment is at the mercy of the carelessness of the pa-

tient. Imagine, for instance, the temptation for a laborer on home treatment, to eat a hearty meal after a hard day's work, when he is feeling perfectly well. This series of cases illustrates the complications of medical treatment, and if the patient will not, or because of ignorance, cannot coöperate, the risks attending medical treatment may well be greater than those of an operation.

The insidious manner in which gastric haemorrhage may overtake a patient is shown by a study of twenty-five such cases studied at another hospital. In twelve cases, hematemesis was the first sign or symptom of any disturbance. In seven cases the haemorrhage was the first indication after complete relief for a considerable time. Four patients were awakened from their sleep by the haemorrhage.

Although physicians may speak of the surgical failures that they are treating medically, this series would indicate that they are fewer than medical failures, whatever the reason may be; in fact, almost all the cases coming to the surgeon will already have tried medical treatment. In deciding whether to operate or not on such cases, it would be well, before giving up medicine, to find out whether the best medical treatment possible for the individual patient has been followed. Finally, medical treatment and advice as to diet should follow operation.

In advising surgical treatment, one must consider the operative mortality. From 1913 to 1922, 265 operations for gastric and duodenal ulcers were performed, with 11 deaths, a mortality of 4.2%. However, in determining the risk of operation in an elective, uncomplicated case of ulcer, it would seem fair to exclude six of these fatalities. One case had perforated, one case with haemorrhage had only a million red blood cells, and four cases were complicated by serious lesions of other organs which required additional operative measures. This leaves 259 operations with 5 deaths. The causes of death in these 5 cases are as follows: There was one death from post-operative pneumonia, and one from a pulmonary embolus. In one case, a duodenal fistula developed, and in another, the stoma failed to function though it was large enough. The fifth case, which showed peritonitis post-mortem, was puzzling. The pathologist reported that "infection was undoubtedly present to a mild degree previous to operation." Including this case, however, there is a mortality of 1.9%.

The five cases which were reoperated upon at this hospital presented an interesting opportunity for study. In one case, the stoma of the original gastro-jejunostomy was placed too high. The result of a gastro-duodenostomy, performed six months later, was still satisfactory when reported nearly two years later. In

another case, gastro-jejunostomy and plication of the pylorus were performed. Nearly two years later, the stoma was satisfactory, but the plication had loosened. Transection of the pylorus gave complete relief, reported two years later. In two cases, after six months and a year, respectively, ulcers had formed at the sites of a gastro-jejunostomy, and of a Heinicke-Miculicz pyloroplasty. Cauterization in one case, and transection of the pylorus with a gastro-jejunostomy in the other, brought complete relief in both cases, reported after two years. In the fifth case, an ulcer had reformed two years after transgastric cauterization. It should be added that in this case, and in a few others, the condition of the patient during the first operation precluded further procedures.

In tabulating the cases in this series treated surgically, the following observations were made.

INCIDENCE BY AGE AND POSITION

	Gastric	Duodenal	Multiple	Total
20-29	4	11	1	16
30-39	8	18	1	27
40-49	13	20	1	34
50-59	10	16	4	30
60-69	5	5		10
Total	40	70	7	117

Both gastric and duodenal ulcers occur most frequently in patients from 40 to 49 years of age. The number of multiple ulcers is small, but it is reasonable that they should occur more often in a later decade. About half the cases of single ulcers occurred in patients more than 45 years of age, whereas about 20% of the national population is composed of persons over this age.

INCIDENCE BY SEX AND POSITION

	Gastric	Duodenal	Multiple
Male	22	56	5
Female	18	14	2
Total	40	70	7

The preponderance of males over females in cases of duodenal ulcer, was shown not to be caused by more frequent failure of women to reply to the follow-up letters, for of 46 failures to reply, chosen at random, 23 were those of men and 13 those of women.

One of the explanations for the greater susceptibility of males to duodenal ulcers is offered by W. Mayo⁹. In the male, the first part of the duodenum passes up, and then down, whereas in the female, the first part is more nearly transverse. Accordingly, the alkaline digestive juices entering the second part can bathe the first part and neutralize the acidity of the entering gastric content more efficiently in the female. Aitken¹⁰ has shown the variation in the positions of the duodenum.

The positions of the gastric ulcers are as fol-

lows: lesser curvature, 25; posterior wall, 10; anterior wall, 3; greater curvature, 1. Almost all the multiple ulcers were in the lesser curvature and duodenum. Duodenal ulcers were seen most frequently in the first part of the duodenum, as is the common observation.

The first symptom noticed was usually general discomfort over the abdomen. Loss of weight was often marked, and should suggest ulcer as well as cancer. Hyperacidity of the gastric contents was by no means a constant finding in cases of either gastric or duodenal ulcers.

In 23 cases of gastric ulcers, the average time for the appearance of pain after meals was two hours; in 32 cases of duodenal ulcers, it was two hours and forty-two minutes.

CONCLUSIONS

1. A study of the results of medical and surgical treatment of gastric and duodenal ulcers at the Peter Bent Brigham Hospital has been made. Of 117 patients treated surgically and followed, 79.5% obtained complete relief, 14.5% obtained partial relief, 5.1% obtained no relief, and 0.9% suffered a hemorrhage. All those obtaining no relief underwent a second operation which was successful in all the cases, four in number, who replied to follow-up letters.

2. In 259 consecutive operations upon elective and uncomplicated cases of gastric and duodenal ulcers, there were 5 deaths, a mortality of 1.9%.

3. Medical treatment is not without its dangers.

4. In choosing between medical and surgical treatment, the intelligence and ability of the patient to coöperate must be considered, as well as the clinical aspect of the case.

5. The findings at later operations which were necessary in five cases are reported, and other observations made in the study are recorded.

The writer wishes to express his gratitude to Dr. Harvey Cushing for permission to make these studies, and to Dr. David Cheever for helpful suggestions.

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DIGESTIBILITY OF OLEOMARGARINE*

BY ARTHUR D. HOLMES

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THE manufacture of oleomargarine dates from 1869, when the French Government offered a prize for a process for the preparation of edible fats suited for table purposes. The object was to furnish sailors and people of limited means with a cheap, wholesome fat of high dietary value. Mege-Mouries¹ attempted to imitate the physiological processes by which milk fat is produced, and eventually obtained a fat which possessed a satisfactory taste, the desired melting point, and the property of keeping for a long time without becoming rancid. It is now known that many details of the process used by Mege-Mouries are unnecessary and, with the development and modification of the process as necessitated by commercial conditions, the oleomargarine industry has increased until 300,000,000 pounds of oleomargarine are produced per annum.

The information at present available regarding the digestibility of oleomargarine by man has resulted largely from the work of European investigators who used the European rather than the American product.

Flurin² determined the digestibility of oleomargarine when eaten in conjunction with a basal ration consisting of boiled meat, buckwheat grits, and white or dark bread, and found in ten experiments that oleomargarine was 94.82% digested. Mayer³ reports that the digestibility of oleomargarine consumed by a 39-year old man and a 9-year old boy was 96.4% and 95.8% respectively. Snyder⁴ in a study of the digestibility of oleomargarine eaten as a part of a ration, found that the average digestibility was for the protein 87.9%, for the fat 94.2%, and for the carbohydrate 97.01%. Luhrig⁵ reports that the digestibility of three grades of oleomargarine was 97.35%, 97.39%, and 97.9%. Wibbens and Hinzenberg⁶ conducted experiments to determine the digestibility of oleomargarine, and found it to be 96.03%. Kienzli⁷ reports that a subject ate 200 grams of oleomargarine daily in conjunction with bread and meat; the oleomargarine was 95.68% digested. Hultgren and Landergren⁸ studied the digestibility of oleomargarine eaten on rye bread and found that 94.45% of the oleomargarine was digested.

*Published with permission of the Secretary of Agriculture.
†The digestion experiments herein reported were a part of the investigation of the digestibility of some seventy edible fats and oils that was conducted by the author while employed as nutrition expert at the United States Department of Agriculture.

Several experimenters have studied the maintenance and growth-stimulating properties of oleomargarine. Ruiter⁹ found that oleomargarine supplied a larger amount of lipoids than any of the other fats studied, and he states that "the high figure for 'margarine proper' may be due to the use of egg yolk besides skim milk as an emulsifying agent."

Drummond and Halliburton¹⁰ report that oleomargarine is able to supply the nutritive requirements of the young rat. Osborne and Mendel¹¹ found that where cessation of growth had resulted from the use of a diet lacking the fat-soluble growth-promoting factor, resumption of growth could be induced by the addition of butter, egg yolk fat, or oleomargarine to the otherwise inadequate diet. During an extended study of the occurrence and nature of the accessory materials essential to a growth-promoting diet, McCollum¹² found that oleomargarine contained a sufficient amount of the fat-soluble growth-promoting substances to meet nutritive requirements.

In this study of the digestibility of oleomargarine, three brands of oleomargarine were selected that represented a range of 8 or 10 cents per pound in retail price. They have been designated Oleomargarine No. 1, Oleomargarine No. 2, and Oleomargarine No. 3. The formulas used in the manufacture of these oleomargarines were supplied to the author, but since oleomargarine manufacturers in common with manufacturers in many industries attach special importance to their own formula and guard against any disclosures regarding the constituents used, no detailed discussion will be included here.

METHODS OF PROCEDURE

The digestion experiments with oleomargarine were conducted by the same methods that were employed in the studies of the digestibility of some seventy fats which have been reported in earlier papers of this series¹³.

DIGESTION EXPERIMENTS

Oleomargarine No. 1

This oleomargarine contained approximately 59% oleo oil, 7% neutral lard, 22% vegetable oils (cottonseed and peanut), and 12% milk fat supplied in the form of butter and skim milk. It was of a golden yellow color, had no pro-

nounced flavor, retailed at the highest price of the three oleomargarines studied, and was of the sort marketed as high grade oleomargarine. The results of the digestion experiments are reported in the following table:

DIGESTIBILITY OF OLEOMARGARINE No. 1

Experiment- Number	Subject	Digestibility of Entire Ration			Digesti- bility of Oleomar- garine	
		Pro- tein	Fat	Carbohy- drate		
515	H. R. G.	58.0	96.2	96.3	79.7	99.3
516	H. A. H.	18.7	86.6	96.6	59.7	91.1
517	P. K.	68.3	93.0	97.4	73.9	96.0
518	C. J. W.	61.4	92.3	96.3	71.3	95.9
779	P. K.	80.0	92.8	97.8	76.7	96.6
780	D. J. M.	72.4	91.4	96.5	66.2	100.0
781	M. L. M.	46.0	88.7	94.4	55.6	98.6
782	J. C. M.	77.0	95.2	96.7	67.6	99.8
783	W. O. C.	74.5	90.1	96.3	67.6	97.2
Average		61.8	91.8	96.5	68.7	97.2

The value 97.2% obtained for the digestibility of this oleomargarine indicates that it is quite completely utilized by the body and compares very favorably in this respect with the well known animal and vegetable fats and oils.

The subjects reported that they considered themselves in normal physical condition during the test periods with oleomargarine from which we conclude that oleomargarine is well tolerated by the body.

Oleomargarine No. 2

The oleomargarine used in the second series of experiments was without characteristic flavor and contained approximately 41% oleo oil, 32% neutral lard, 24% vegetable oil (peanut), and 3% milk fat which was derived from cream and skim milk. This sample of oleomargarine was considered as being typical of a second grade oleomargarine. Its digestibility was studied in seven tests.

DIGESTIBILITY OF OLEOMARGARINE No. 2

Experiment- Number	Subject	Digestibility of Entire Ration			Digesti- bility of Oleomar- garine	
		Pro- tein	Fat	Carbohy- drate		
523	H. R. G.	62.4	94.1	96.4	78.6	97.8
524	A. J. H.	34.0	85.3	97.0	60.7	89.6
525	P. K.	65.9	90.1	97.5	73.3	93.5
526	C. J. W.	72.9	93.8	97.3	80.7	96.7
590	P. K.	73.2	85.9	97.8	83.9	88.9
591	J. C. M.	27.4	89.7	92.8	55.5	96.8
592	C. J. W.	48.7	85.4	95.3	70.3	90.3
Average		54.9	98.2	96.3	71.8	93.4

Five different subjects assisted in the seven experiments here reported in which the average digestibility of a medium grade oleomargarine was found to be 93.4%. The average amount of fat consumed in these experiments was 80 grams

per man daily; in one instance, experiment 592, subject C. J. W., ate 125 grams for three consecutive days without experiencing any physiological disturbance. This would indicate that this type of oleomargarine does not produce any laxative effect when consumed in amounts not exceeding 125 grams daily.

Oleomargarine No. 3

A white (uncolored) oleomargarine was studied in the third series of experiments. Its composition was somewhat different than that of the others since it contained no neutral lard. The constituents used in the preparation of this sample of oleomargarine were; oleo oil 67%; vegetable oil (cottonseed) 33%; and milk fat 0.1%.

Four different subjects assisted in the study of this sample of oleomargarine, and the usual uniform and standardized methods developed for the determination of the digestibility of edible fats were maintained throughout the test periods, the results of which are reported in the following table:

DIGESTIBILITY OF OLEOMARGARINE No. 3

Experiment- Number	Subject	Digestibility of Entire Ration			Digesti- bility of Oleomar- garine	
		Pro- tein	Fat	Carbohy- drate		
531	H. R. G.	69.2	94.6	96.3	85.0	97.8
532	A. J. H.	58.0	94.1	97.8	82.5	96.3
533	P. K.	69.7	93.7	97.3	80.1	96.6
534	C. J. W.	55.2	92.7	96.5	63.5	96.6
Average		63.0	93.8	99.3	77.8	96.8

The digestibility of this sample of oleomargarine was found to be 96.8%, a value which was to be expected since the oleomargarine consisted of 67% oleo oil¹⁴ whose digestibility has been shown to be 96.8%, and 33% cottonseed oil¹⁵ whose digestibility was found to be 97.8%. The average value, 96.8% obtained in the above experiments indicates that the sample of oleomargarine under consideration in these tests was well assimilated by the body.

DISCUSSION

Twenty digestion experiments were conducted with human subjects to determine the digestibility of typical samples of three grades of oleomargarines containing animal fats.

The three grades of oleomargarine contained different amounts of milk fat which was supplied from butter, cream, or milk.

The coefficients of digestibility obtained for the oleomargarine under consideration were 97.2%, 93.4%, and 96.8%.

The protein and carbohydrate supplied by the diet were as thoroughly digested as in the earlier studies of the digestibility of other edible fats in which the same basal ration was used, giving

added evidence for the belief that edible fats do not exercise any marked effect upon the digestibility of the other constituents of the diet.

The subjects reported that they experienced no physiological disturbance during any of the test periods with oleomargarine. And since the diet produced no laxative effect, it may be concluded that the limit of tolerance is in excess of 125 grams, the highest average amount eaten per man per day in any of the series of experiments here reported.

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NEW ENGLAND SURGICAL SOCIETY

SOME NEW ITEMS AS TO HIP FRACTURES*

BY FREDERIC J. COTTON

HIP FRACTURES, as I am almost tired of saying, fall clearly into two classes,—the extracapsular, which call for decent skill and care to avoid deformity, which cannot be kept from uniting, which are not a problem; and intracapsular fractures, which anciently united when they happened to be impacted, and if the impaction happened not to give way.

Most of them did rather badly—many could not have done worse. They still are a problem, for though we do better with them now, there are many failures, and the only man who has none is he who scorns end-result investigations.

It is still too early to present what I am still working on, namely—the end-result statistics of artificial impaction. In-so-far, the title of this paper is misleading.

What I am presenting here is, first, a small series of cases in which one special problem was attacked—namely, that of excessive absorption with the prospect of loss of the original impaction.

Those who have used continuous "check" X-rays know that in a proportion of cases (not small) the softening (which always occurs in every fracture) is excessive; not rarely, despite all care,—and in any position, the impaction is spoiled, and the fragments fall apart.

How is this to be helped?

Last spring, encouraged by results in promoting active hyperaemia, and thus helping union in long bone fractures with delayed repair processes (reported to this Association last year) I tried diathermy—or rather Dr. F. B. Granger tried it out for me, on three cases that I had transferred to the New England Hospital for Women and Children, where this treatment could be carried out.

The series is too short to be conclusive, but

the results were excellent, with bony union in all three cases, results good enough to make me go on with it and recommend it to your attention in the cases that threaten to "come apart."

Diathermy calls for a chance to put in electrode pads, but this means only windows that do not appreciably weaken the cast. By having a good nurse do the detail work, under supervision, as we did, daily application is practicable.

I am going farther with this, but hope others will try it out, and report results. Am so encouraged about these cases that I am ready to hand it to you without waiting for really conclusive proof. Diathermy can do no harm in these cases, certainly, and I think it saved one or two of this little series from the cripple's fate.

The other thing I want to talk about is late impaction of loose fractures of the neck of the femur.

Long as I have been doing, and talking about, artificial impaction, I had always supposed it feasible only within the first week or so. One thinks of fracture surfaces as "sealing off" open ends, just as a grapegrower's cuttings do in his sand box.

CASE I

But on March 29, 1923, I had put up to me an untreated hip fracture, intracapsular, loose, nearly seven weeks old. She had had no treatment, or whereabouts, until Dr. W. P. Cones was called, and called upon me to help.

The patient was elderly, frail, in no shape to stand an open operation. She had work of some importance to do, was intelligent and courageous, and demanded a decent hip all the more because the uninjured leg was not much of a leg as a result of childhood infantile paralysis.

*Read before the New England Surgical Society at Hartford, Conn., September 26, 1924.

So I took a chance—reduced under ether, impacted with the mallet, and treated in the routine way.

That is two years now—she has finished and published her book, and is hopping around as lively as ever on this leg. Union is bony, function practically perfect.

CASE II

Next, a loose fracture which had been properly and carefully treated with a plaster spica in the "Whitman position."



This treatment had utterly failed.

I saw her March 29, 1923, with Drs. I. B. Walker and Otto Hermann.

The fracture had "fallen apart."

In spite of the ten weeks elapsed, it seemed to me worth while to try what had succeeded in Case I.

Reduction by traction in abduction, impaction with the heavy mallet, application of my double spica in abduction, and, especially in sharp internal rotation, were carried out by Dr. O. J. Hermann.

I did not see her again until April, 1924, when, to my delight, she showed a negligible shortening, fair motion, obviously solid union.

September 23, 1924, I finally found her again, just after her return from "the Beach," walking almost without limp with excellent power and control. Shortening—as near as I could measure— $\frac{1}{4}$ inch.

Flexion to 60 degrees only, and knee flexion short of a right angle. This will mend, the hip fracture has very serviceably mended.

There is no doubt of the bony union, I think, though my rediscovery of this patient is too

recent for me to show you end-result X-rays. They will probably be to hand before this note gets into print.

CASE III

This was a woman of sixty, brought to me a bit late after injury twelve days after she sustained her fall. I reduced displacement and did the routine impaction and fixation in double spica, in abduction and internal rotation.

By reason of defective Ward care, or for no reason, union failed, and after fourteen weeks I again reduced, impacted and put her up corrected.

This is one of the cases I transferred to get diathermy treatment, previously noted.

For one or the other reason she is now walking with one crutch, with bony union, none too good, perhaps, in its massiveness of bone.

Perhaps this case is not an absolutely assured success but it looks it, and at all events bony union is present.

CASE IV

The fourth case, a young man of 22 years, was hurt Oct. 26, 1923, reduced and put up in a "Whitman" spica by Dr. J. W. Sever, Oct. 27, 1923. Cast off Dec. 29.

When I saw him Jan. 6, 1924, the fracture had obviously fallen apart.

That was ten weeks after injury.

It seemed hopeless, but, mindful of the first three, I decided to take a chance.

January 6, 1924, under ether, the leg was dragged down, inverted, impacted with the 8½ lb. mallet, put up as usual.

Today union seems unquestionably bony. There is 5/8 inch shortening.

What he can do he will show you.

Later I will show you the X-rays.

All that these cases *surely* prove is that repair in loose intracapsular hip fractures may be effective, though late.

Beyond this I suspect they show that artificial impaction may be used to "start a fresh deal" by crumpling up and coaptating fracture surfaces already perhaps partly scummed over.

Take them for what they are worth until we get others!

At the least they show that we can do something for a class of cases seen late that looked hopeless that we can do this in a proportion of cases not yet known, within time limits not yet established, but surely beyond anything seriously considered until now.

DR. WILLIAM C. PETERS, Bangor: When I was invited to discuss Dr. Cotton's paper, I replied that I could not do it for although I see many cases of hip fracture in the woods of Maine I do not feel like giving any advice about treatment to the gentlemen of this Society.

Occasionally I have sent to me cases of old,

loose intracapsular fracture of the hip in which the doctor who had charge of the initial treatment was sure that they started as impacted fracture. Such cases are examples of the absorption of callus, followed by a secondary mobility at the seat of fracture.

I have nothing to add to Dr. Cotton's remarks in regard to Artificial Impaction but there is one point I should like to emphasize in connection with the treatment of these hip fractures and that is immobilization. General practitioners are apt to treat this matter lightly. The patients are usually advanced in years and as the impaction feels firm all that is considered necessary is a sand bag or two. The older the patient the more necessary careful immobilization and if carefully managed they will stand this very well. I use the plaster spica, carefully padded and continue it for a long period with very satisfactory results.

I should like to ask Dr. Cotton the age of the various patients upon which he has done artificial impaction.

DR. F. B. LUND, Boston: In our hospital I can testify to how much good Dr. Cotton's methods have done, and we are learning from him; and having him on the staff has been very valuable to the large fracture clinic at the City Hospital. We should be glad to hear further discussion of the paper.

DR. E. L. HUNT, Worcester: I would like to have Dr. Cotton tell us about his technique in that mallet impaction.

Question from a member: I would like to ask if he has given up the treatment by bone splints or bone plates.

DR. F. J. COTTON, Boston (closing): In the first place, as to the age—the first patient I can't tell you, "she was that old." She was well into the sixties. The second one was 48 and the third one 60, and this fellow whom I have shown is only 22.

What Dr. Peters says about the length of time—there is no question about it. He is right. These things to get repair take longer than we think, and it is a matter of a great many months; and I am not prepared to say that these three cases would have had to be done over again, if they had been kept up. They had three months of absolute impaction and had not repaired. So heaven knows what might happen in the way of repair in these late cases.

I had an interesting communication from Dr. Ruth of Des Moines. We handled case out there in which there had been non-union in a fracture of the base of the neck, the only case I had ever seen, and it persisted in a non-union for eighteen months, and finally it was discovered that she had a 4 plus Wassermann and then under treatment it turned around and united. That was a fracture of the base.

I looked up the cases at the City Hospital and found that many of them had flail joints, and I think it wasn't due to faulty observation but that they fell apart.

The question about the technique—I haven't been breaking up the cases of favorable impaction. Please remember that. I am not going to do anything in a case like that except throw it over in a position of abduction and sharp internal rotation to the point of resistance; but other than that I am not going to do any more in cases in decent position, but in cases in which the impaction is useless I am going to break and reimpact.

I get the patient on a table and drag the thing down with my foot in the crotch. With the help of an assistant who does the holding and makes counter pressure, I then, with a padding of felt and a mallet weighing eight pounds and a half, pound on the trochanter with a swinging blow and with much force, and I have never done any harm—not even an ecchymosis; and when you have done that a few times, you will find that the fracture is no longer loose in your hands, it doesn't flop over and you have a sense of the penetration; there is no way of telling the distance of the impaction, but it is probably not over an eighth of an inch but it gives you coaptation and then you get the patient up in a spica and you have it straightened out and give it a chance to go ahead with the repair process.

I am not ready to talk about statistics but I have been getting results with only an occasional failure. Prior to that you know what you got with loose fractures of the hip, and I guess everybody got the same thing.

THE JUSTIFICATION OF ENFORCED HOSPITALIZATION

Gradually the public has awakened to the value of the Municipal Contagious Disease Hospital. It has a distinct and vital function. Occasionally, some one who has sinned against the health laws, makes an outcry that the Department of Health is arbitrary in enforcing hospitalization of a contagious disease patient. It is a vested authority of the Commissioner of Health to meet any threatening contagion or violation of the health laws that endanger the community as a whole, in any manner thought best to combat it. What seems like a forcible detention is nothing more than a sure quarantine. Fortunately, this procedure is becoming less frequent. There is greater cooperation on the part of the public and the majority of the patients in the Municipal Contagious Disease Hospital is now voluntary. This is a hopeful sign for the day when people will have their contagious diseases cared for in a hospital specially equipped for that purpose.—*Bulletin Chicago Dept. of Health.*

Case Records
of the
Massachusetts General Hospital

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN
WEEKLY CLINICO-PATHOLOGICAL EXERCISES

EDITED BY

RICHARD C. CABOT, M.D., AND HUGH CABOT, M.D.
F. M. PAINTER, A.B., ASSISTANT EDITOR

CASE 11251

MEDICAL DEPARTMENT

A German truck driver of nineteen entered the hospital March 19 complaining of penile and scrotal sores of three months' duration. He gave a history of influenza six years before admission and frequent sore throats. Six years before admission after riding a bicycle he had dysuria for a period. For several years he had had frequent attacks of dizziness on change of position, with specks before the eyes. He had night sweats. For a year he had urinated three times at night and had taken a good deal of water at night. For five months he had had cardiacl pain like pins and needles. He had some shortness of breath on exertion. For three weeks he had had piles with a little bleeding.

He gave a history of exposure to syphilis followed by the lesions found on examination.

Examination showed a well nourished young man with a general macular eruption and papules and scaly psoriasiform lesions on the extensor surface of the arms and elbows. The buccal mucosa showed small mucous patches. The tonsils and uvula were very large. The throat and pharynx were congested. The left tonsil showed mucous patches. There was glandular hypertrophy, especially in the cervical and inguinal chains. The right epitrochlears were palpable. The heart showed no abnormalities except that the left border of dullness was one centimeter outside the midclavicular line. The apex impulse is not recorded. The scrotum and anus showed several large condylomata. The shaft showed eruptive lesions and the glans and sulus three or four lesions. The reflexes were normal. The pupils reacted to light but not well to distance.

The chart is not remarkable except for a drop of temperature to 96.5° March 22, the day of injection of 0.3 grams of diarsenol. The urine was cloudy, the specific gravity 1.028, no albumin or sugar. The amount is not recorded. The hemoglobin was 75 per cent, the leucocytes 12,100.

Under antisyphilitic treatment the condylomata improved and the rash faded. Following his discharge March 26 he was given a course of arsphenamin and gray oil, ending

October 21. He felt perfectly well during the treatment.

February 21 he reentered the hospital complaining of pain in the left lumbar region of two weeks' duration. This was worse when he lay down, though he felt it somewhat during the day. For two weeks he had had acute tonsillitis and mild headaches. February 11 his face and ankles showed edema which went down but reappeared the day of admission. For a week or two he had had dimming of vision and floating scotomata. He had cramp-like pains in the extensors of the thighs when he walked. The penis and scrotum were swollen. During his illness his urinary output had been small compared with his fluid intake. His bowels, which were usually very regular, were constipated.

Upon examination he appeared pale and rather ill. The eyelids and face in general were puffy. There was marked injection of the pharynx, pillars and tonsils. The tonsils were swollen. The cervical glands were bean-sized, soft and slightly tender. The heart showed no enlargement to percussion. The rate was slow. The aortic second sound was accentuated. The pulses and arteries were normal. The blood pressure was 105/70 to 130/85. The abdomen was tense, with voluntary spasm and some distension. The abdominal wall was edematous. There was dullness in both flanks and fluid wave. Palpation was not satisfactory. The scar of the old penile primary was seen in the coronal sulcus. There was moderate edema of the penis and scrotum, and slight pitting edema of the shins and ankles. The knee-jerks and ankle-jerks were normal.

The temperature was 96.8° to 101.3° with a terminal rise to 106.3°. The pulse was 55 to 90 with a terminal rise to 142. The respiration was normal except for a rise to 34 two days before death. The urine was normal in amount except for an output of sixty-five ounces March 6 and ten ounces four days before death. A Schlayer test showed no marked fixation of gravity (1.032-1.040). There was chlorid retention but good ability to concentrate. At all of fifteen other examinations the urine showed a trace to a large trace of albumin, and rare leucocytes to masses of leucocytes; until March 11 no red blood corpuscles, afterwards rare red cells at five of ten examinations. February 22 and 28 the renal function was thirty-five per cent., March 7 thirty per cent. The hemoglobin was 90 to 75 per cent., the leucocytes 8,300 to 29,000, polynuclears 71 per cent., reds normal. The non-protein nitrogen March 2 was 33 mgm., March 6, 9 and 14 29 mgm., April 25 60 mgm. Hematocrit cell volume 58 per cent. Total plasma protein by Kjeldahl's method 4.5 per cent., by refractometer 4.7 per cent. (using globulin factor). CO₂ combining power April 16 20.7 per cent. (There was much fat in the plasma.) Two Wassermanns were negative.

X-ray showed no kidney outlines visible on either side. Two shadows on the right a little outside the usual kidney area were thought to be probable artefacts. March 5 a lumbar puncture gave an initial pressure of 200, 6-10 cells, total protein 7, Wassermann negative, goldsol 1335542100. March 7 an abdominal tap gave 44 ounces of translucent milky fluid, specific gravity 1.008, cell count, reds 40, leucocytes 20, 95 per cent. lymphocytes, 5 per cent. polymorphonuclears. Culture showed no growth. Protein on the abdominal fluid 150, on plasma 3926. Non-protein nitrogen on fluid 22, on plasma 23. The chlorids, as NaCl, on the fluids 607, on plasma 535. Cholesterol too low to read. Fat in the fluid 260, (plasma 1,480.) March 19 another tap gave eight pints of opalescent milky fluid culture from which showed a few staphylococci. March 23 a third tap gave 4500 c.c. of similar fluid. Culture gave no growth. March 28 a tap gave 6,500 c.c. of similar fluid, April 9 7,400 c.c. The last gave a non-protein nitrogen of 30 (plasma 28), chlorids 691 (plasma 609). April 12 another tap gave 5,500 c.c., April 18 10,000. The chemistry of the later fluids showed no change except the progressive rise in chlorids accompanying the intake of ammonium chlorid.

On a salt free diet and sharp limitation of fluids the patient showed a rapidly increasing edema, seven pounds in two days. By increasing the fluid intake slight diuresis was obtained. After the plasma protein tests March 6 an increasing protein diet was started. No improvement followed in the next four days. X-ray of the teeth and sinuses was negative. March 13 the protein feeding was stopped on account of an attack of vomiting. March 16 he was started on serum albumin grams 1x daily by mouth. He became distinctly worse. In three days ending March 23 he gained ten pounds and had absolutely no increase in output. His ascites collected so rapidly that he had required tapping twice in the past week. The plasma proteins had fallen rather than risen. March 28 theocin was started, ten grains that day, twenty the following day, and ten March 30.

April 5 he complained of deafness in the right ear when he sat up. The membrane was reddened. There was retraction of the drum. An ear consultant believed the patient had had an acute process which was quieting down and advised no treatment.

April 7 ammonium chlorid was started, one gram per hour up to a total of eight grams per day. There was no effect that could be seen except the slight diuresis for one day April 11. The ammonium chlorid was stopped April 17 because the blood CO₂ was down to 20.7 per cent.

The morning of April 23 the patient awoke with abdominal cramps and diarrhea which lasted all day. An ear consultant reported,

"Ear discharging three days. Slight pain now. No mastoid tenderness at present. History of nausea and vomiting, dizziness and chill this morning. The patient has an acute suppurative otitis media, with possible further involvement, according to the morning's history." Hot saline irrigations were ordered. Examination showed a sense of resistance in the right upper quadrant; no true spasm. April 24 another aurist found the ear in the first stage of a purulent otitis media. Smear from the pus from the ear showed questionable staphylococci. A blood culture showed streptococcus hemolyticus. The patient complained of marked tenderness in the right costovertebral angle. April 26 he died.

DISCUSSION

BY DR. RICHARD C. CABOT

NOTES ON THE HISTORY

This pupillary reaction is the opposite to the Argyll-Robertson, and is not significant so far as I know.

At the first entry I do not see that we have any reason to consider anything in particular except syphilis, apparently treated with success.

He comes in now for the second time with something suggesting nephritis.

NOTES ON THE PHYSICAL EXAMINATION

There is an extraordinarily rapid accumulation of fluid here, more at each tap and with shorter intervals between taps.

I suppose the record means that there was no increase of urinary output. Diuresis is a bad term for that which we have fallen into the habit of using.

DIFFERENTIAL DIAGNOSIS

There is a great deal here that I do not know enough to say anything in particular about. What appears is that he had a blocked kidney of the type which we call nephrosis rather than nephritis. But the lesion perhaps depends on his syphilis, and so for all I know may be of the amyloid type. I do not know any way to distinguish an amyloid kidney from a nephrotic.

He evidently has not nephritis of the ordinary type. He has good concentration. He has a good output of phthalein. But he accumulates edema at an extraordinary rate, has a lot of fat in his blood, and finally gets a streptococcus infection involving probably various parts, exactly what I do not know unless possibly the kidney.

Can you add anything on the chemistry of this situation, Dr. Field?

DR. HENRY FIELD, JR.: The protein in the plasma is low—I think that is the striking thing—something under four per cent. instead

of close to seven per cent. That is characteristic of nephrosis as well as of other types of nephritis.

DR. CABOT: Did anybody have any explanation of why it should be low?

DR. FIELD: It is low in nephrosis, and that is the basis of Epstein's recommendation of a high protein diet. But apparently a high protein diet did no good in this case. The protein in the plasma was not increased and he got no diuresis such as Epstein reports. We have not been able to obtain such in similar cases.

DR. CABOT: He apparently had some acidosis.

DR. FIELD: That was as a result of treatment, a therapeutic acidosis due to chlorid given in an effort to cause diuresis.

DR. CABOT: I do not think I can say anything more about this case. I see no reason to suppose any disease except of the kidney, resulting in a terminal streptococcus sepsis. That sepsis we know of in the ear and we hear of some pain in the right upper quadrant and right costovertebral angle which may have been due to the sepsis. That makes us think of the right kidney, but it is too scanty evidence to point to anything in particular.

Streptococcus sepsis is not so likely to involve the kidney as the serous membranes. Pericarditis, peritonitis, pleuritis and inflammation of joint membranes are what we expect when the streptococcus is found in the blood. I take it his ascites is not due to any local lesion, but is part of his generalized edema and depends on this kidney trouble.

DR. FREMONT-SMITH: Is there anything you can add to the discussion of this case? I have said that this is not an ordinary nephritis but has characteristics of what we call nephrosis so far as I know them, yet coming after syphilis in this way one might perfectly well think of amyloid. I do not know any differential between amyloid kidney and the kidney called nephrosis.

DR. F. FREMONT-SMITH: Dr. Marriott has called attention to the association of staphylococcus infections with this type of kidney involvement, the so-called nephrosis, as distinguished from the streptococcus infection associated with the ordinary glomerulonephritis that we see where there is nitrogen retention and low renal function. In your experience has that been the case?

DR. CABOT: No, I have never seen anything like this with staphylococcus kidneys.

DR. F. FREMONT-SMITH: I do not mean staphylococcus infections of the kidney but chronic staphylococcus infections in other parts. We have had one case clinically similar that did not come to post-mortem but had chronic staphylococcus osteomyelitis, and I have seen one other case at the City Hospital. It is rather interesting that this man had an ear lesion that appeared only toward the end,

from which we grew staphylococcus. The staphylococcus was terminal, but previous to that he had been complaining of the ear off and on for two weeks. Consultants from the Eye and Ear Infirmary came to see it and in cultures we finally obtained a non-aureus staphylococcus from the ear. I do not know that that has any real bearing on the case.

CLINICAL DIAGNOSIS (FROM HOSPITAL RECORD)

Chronic nephrosis.

Acute otitis media.

Septicemia.

DR. RICHARD C. CABOT'S DIAGNOSIS

Nephrosis.

Terminal streptococcus septicemia.

ANATOMICAL DIAGNOSIS

1. Primary fatal lesion

Chronic nephrosis.

2. Secondary or terminal lesions

Purulent otitis media with purulent mastoiditis, right.

Septicemia, streptococcus hemolyticus.

Edema of the lungs, with focal pneumonia lower lobe right lung.

Serofibrinopurulent peritonitis.

Soft hyperplastic spleen.

Wet brain.

Slight edema of the extremities and scrotum.

3. Historical landmarks

Slight chronic pleuritis, right.

DR. RICHARDSON: The pia showed much infiltration with thin pale fluid. In the region of the right middle ear there was a collection of pus, and in the right mastoid in the region of the middle ear there was also infiltration of pus into that bone; purulent otitis media and purulent mastoiditis on the right. The brain weighed 1310 grams, and other than for edema was negative.

The skin and mucous membranes were pale. The feet, ankles and scrotum were swollen and pitted on pressure. There was some edema of the hands and arms. In the anterior abdominal wall between the umbilicus and the pubes there were several tap wounds.

The peritoneal cavity contained 1500 c.c. of thin cloudy fluid and fibrin and in many places smaller and larger masses of mucopurulent material, the coverglass from which showed streptococci and leucocytes,—a serofibrinopurulent peritonitis. This exudate was in good amount in the lesser peritoneal cavity and extended along the pancreas over to the region of the left kidney. The appendix was negative. The gastro-intestinal tract was negative. The mesenteric and retroperitoneal glands were

slightly enlarged but on section negative.

In each pleural cavity there was a small amount of pale clear fluid. There were a few pleural adhesions on the right, none on the left. The bronchial glands were somewhat enlarged, reddened, soft and juicy. The right lung in the region of the apex was negative. Midway posteriorly to the right there were a few small foci of gray-red pneumonia. There was some edema of the tissue. The left lung showed considerable edema but no areas of consolidation.

The spleen weighed 405 grams,—considerably enlarged, the tissue purplish-brown-red, soft and mushy.

The kidneys weighed 595 grams. That is of course considerably enlarged. The surfaces were rounded, the capsules were closely applied to the organs and in one or two places there were some faint adhesions, but generally the surfaces were smooth. On section the tissue generally was plump, swollen, wet, the cortex and pyramids were made out, and the cortex was very wide, generally at least ten millimeters or more. The section surfaces were pale brownish in color, rather homogeneous. The mucosa of the pelvis showed scattered over it many minute hemorrhagic areas.

Culture from the blood in life yielded the streptococcus hemolyticus. The coverglass from the purulent material in the peritoneal cavity showed streptococci and leucocytes, so that at least there was a streptococcus infection at the end.

The kidneys microscopically showed many of the cortical tubules larger than normal, with larger and smaller epithelial cells, many of which were crowded with hyalin globules of varying size. The tubules contained much detritus and many hyalin casts. The glomeruli contained granular material in the capsular spaces. The pyramidal tubules were negative except that some of them contained casts. There was no increase in the connective tissue.

DR. CABOT: Was there any amyloid?

DR. RICHARDSON: No.

DR. CABOT: Do you know whether they thought during life that this condition was related to the syphilis or was independent?

DR. FIELD: I think it was the consensus of opinion that it was not related to the syphilis.

DR. CABOT: And the etiology was not known. How much did this look like a mercurial nephritis in gross?

DR. RICHARDSON: Not like it. It looked like a wet kidney with this marked degeneration of the tubular epithelium, casts, and an extremely wide cortex and increase in weight.

DR. CABOT: Have you seen this condition associated with any particular poisoning?

DR. RICHARDSON: Not a kidney just like this. It makes us think, of course, of the edematous kidneys we find once in a while. It may be that there is some relation between this condition which we call nephrosis and those big

edematous kidneys which are, so far as definite changes go, negative.

DR. CABOT: So on the pathological side you have nothing to say as to the etiology?

DR. RICHARDSON: No. The question of the association with syphilis has been raised, but no spirochetes were found in the kidney sections.

DR. CABOT: There is no evidence of syphilis elsewhere in the body?

DR. RICHARDSON: No.

DR. FRANK FREMONT-SMITH: Can Dr. Richardson tell us whether the mastoid was an acute or a chronic process?

DR. RICHARDSON: The process had invaded the mastoid bone and appeared to be subacute.

DR. FREMONT-SMITH: We were particularly interested in the mastoid, as we recovered from it a pure growth of staphylococcus a few days before he died, and thought that this might be the chronic staphylococcus focus that Marriott has called attention to.

CASE 11252

MEDICAL DEPARTMENT

A colored houseman of thirty-three entered March 24. He gave a history of boils in childhood, whooping cough, gonorrhea years earlier, a sore on the penis twelve years before admission, and an attack of "rheumatism" the previous winter. His habits were good. Three months before admission he began to have heavy dull ache across the upper abdomen and dyspnea on exertion. The ache persisted and the dyspnea grew steadily worse until at admission it was continuous and at times he had to sit up to get his breath. During the past two months he had had cough and raised a great deal of bloody sputum. For the past month his legs had been swollen. He had some palpitation, slept poorly, had little appetite, and during the past week had vomited food immediately after eating. He had been using salts with small movements. For four weeks he had been unable to work and for three weeks had been in bed.

The examination showed a well nourished man with cyanotic mucous membranes. The throat was covered with mucus. The apex impulse of the heart was felt in the sixth space five inches to the left of the midline. The left border of dullness was four (?) inches to the left, the right border of dullness an inch and a half to the right of the median line. The action was rapid. The pulmonic second sound was accentuated, the aortic second sound absent. A short soft systolic murmur and a soft diastolic murmur were heard at the apex, a loud diastolic and a systolic all over the precordia, loudest at the third left interspace. There was a diastolic murmur in the aortic area and also in the back. There was Corrigan pulse, pistol shot and Duroziez's sign.

The lungs showed slight dullness at both bases and medium moist rales throughout, more numerous at the bases. Expiration was prolonged and harsh. There was slight shifting dullness in the flanks and general tenderness throughout the abdomen, more marked over the liver, which extended to three inches below the costal margin, where the edge was felt in the mammillary line. The splenic dullness was not made out. The edge was indistinctly felt. A few bean-sized glands were felt in the axillae and groins. The pupils were normal. The knee-jerks were unsatisfactory, the plantars normal. There was marked edema of the ankles, legs and thighs. There was a subcutaneous mass four by six inches over the lower ribs in the left back.

During his twelve days in the hospital the temperature gradually rose from 97.1° to 103.2°. The pulse ranged from 101 to 135, the respirations from 16 to 39. The urine was from 34 to 92 ounces, specific gravity 1.012-1.016, a slight trace to the slightest possible trace of albumin at all of three examinations, a rare blood cell at one. The hemoglobin was 100 per cent., the leucocytes 14,000 to 19,300.

The patient failed from admission. After the first day the sputum was almost pure blood. No localizing sign of an infarct could be found. The edema of the legs and genitals increased. March 29 there was a patch of bronchial breathing just below the angle of the right scapula which increased, extending to the midscapula by April 3. That day, after he had been delirious for several days, he died.

DISCUSSION

BY DR. MAURICE FREMONT-SMITH

NOTES ON THE HISTORY

The history suggests the rather rapid onset of cardiac decompensation, and it is interesting to note the first symptom,—pain in the upper abdomen, probably due to congestion of the liver with stretching of the capsule.

NOTES ON THE PHYSICAL EXAMINATION

The most definite sign that we have here as to the size of the heart is the apex impulse in the sixth space. In other words, we know that he has a heart enlarged downward.

"Aortic second sound absent" is of importance, especially if one were trying to make a diagnosis between aortic stenosis and aneurism. In aneurism the second sound is present. We know at any rate that the aortic valve is badly damaged. We are not so sure as to the mitral valve. From the description here I think we are likely to be right if we say that there is no mitral stenosis, that the diastolic murmur at the apex is the Austin Flint murmur that occurs with aortic regurgitation.

With regard to the localization of the murmur in aortic regurgitation it is interesting to re-

member that there are times when one may have a Corrigan pulse and a zero systolic blood pressure and yet find no diastolic murmur in the aortic area, and that that aortic diastolic may be picked up elsewhere in the chest, even in the axilla. I remember one such case at the Brigham Hospital.

I do not know how much attention is being paid now to splenic dullness. I have always felt myself that unless a spleen could be felt a diagnosis of enlargement was very questionable, and if one did find the dullness enlarged I doubt whether that would be sufficient in itself to be of any significance. I think that is a question that it would be interesting to discuss.

Wherever one finds enlargement of the lymphatic glands it has to be explained.

Of course we should like to have a blood smear here. That is not given to us. Such glands may be of no significance, but it is very much safer to attempt to explain enlargement of the glands.

We have hardly enough description to make it possible to guess what the subcutaneous mass might be,—probably a fatty tumor. We should have to think of the possibility of von Recklinghausen's I suppose, although such masses occur on the scalp usually.

There is nothing in the urine that would not be explained by chronic passive congestion.

We should like to know how much sputum there was. A very little sputum almost pure blood might perhaps occur after a pulmonary infarct, although the amount of blood in the sputum in pulmonary infarct is small.

MISS PAINTER: At the first record it was small in amount; the second record does not specify.

DR. FREMONT-SMITH: He might well have some blood in his sputum from chronic passive congestion of his lungs, and then he is evidently developing a pneumonia.

DIFFERENTIAL DIAGNOSIS

I think there is rather little to discuss. We have a badly damaged heart in a man of thirty-three, with progressive myocardial failure, all the evidence of chronic passive congestion and the final development of a patch of bronchopneumonia.

On the evidence given I think it is impossible to state definitely what type of heart injury this man had. It lies between luetic and rheumatic cardiac disease. I think we have a right to lean toward the luetic side, and I believe that we shall find syphilitic heart disease and all the evidence of chronic passive congestion and an area of bronchopneumonia.

DR. CABOT: I agree with Dr. Fremont-Smith about percussion of the spleen. In cases where we do not feel it I think percussion is of no use.

I am interested too in the points he spoke of. I think I have seen a number of patients with every indication of syphilitic disease of the

aortic valve, the patient's complaint being abdominal pain to a greater degree than the necropsy findings would very well explain. I am not sure it is all chronic passive congestion of the liver. It seems to me we see more pain in heart disease of syphilitic origin than we can explain.

A PHYSICIAN: Would you pay any attention to this note that the murmurs were better brought out by pressure?

DR. CABOT: That is an old trick we used to try. It is true of all murmurs. We use a Bowles stethoscope, with which we can get considerable pressure without hurting the patient, and we can make any murmur louder in this way.

A PHYSICIAN: But more marked with a friction rub.

DR. CABOT: That is a different thing, because there we can get nearer to the thing and affect the physical surface of the thing concerned. But with the heart I do not think this concerns us at all.

CLINICAL DIAGNOSIS (FROM HOSPITAL RECORD)

- Aortic roughening.
- Aortic and mitral regurgitation.
- Failing compensation.
- Possible pericarditis.
- Chronic passive congestion.
- Infarcts of the lungs and bronchopneumonia.

DR. MAURICE FREMONT-SMITH'S DIAGNOSIS

- Syphilitic heart disease.
- Aortic regurgitation.
- Chronic passive congestion.
- Bronchial pneumonia.

ANATOMICAL DIAGNOSIS

1. Primary fatal lesion

- Marked fibrous endocarditis of the aortic valve
- and slight fibrous endocarditis of the mitral valve.

2. Secondary or terminal lesions

- Hypertrophy and dilatation of the heart.
- Streptococcus septicemia.
- Focal pneumonia.
- Hemorrhagic edema and infarcts of the lungs.
- General chronic passive congestion.
- Anasarca.
- Hydropericardium.
- Ascites.

3. Historical landmarks

- Chronic perisplenitis and hepatitis.
- Foci of necrosis in the fat tissue of the pancreas.

DR. RICHARDSON: The lower extremities were swollen and pitted on pressure. There was considerable ascites. The liver was three fingers be-

low the costal border. The diaphragm on the left was at the fifth rib, on the right at the fifth interspace.

On the right the pleural cavity showed purulent pleuritis. The lungs showed chronic passive congestion and intermingled with tissue of that sort were definite areas of pneumonia and in places infarcts.

The usual sources for infarcts in the lung were wanting in this case. There was nothing in the appendices, nothing in the right side of the heart. The vessels were opened and nothing was found in them. That brings up the question as to whether there can be hemorrhagic infarction of the lung without anything visible in the vessels. This case would seem to say so.

The bronchi contained much mucopurulent material.

There was a slight hydropericardium. The heart weighed 455 grams, moderate hypertrophy, with a good myocardium, on the left 13 mm., on the right five. The left ventricle was full thickness and the right thicker than usual. The cavities were dilated. The mitral valve circumference was ten and a half cm., the aortic seven, the tricuspid fourteen. The mitral valve showed a slight amount of chronic fibrous endocarditis extending in one place slightly up on the auricular wall. The aortic valve showed marked fibrosis with decrease in the width of the cusps and deformity of the valve. The aorta showed only a slight amount of arteriosclerosis—a chronic endocarditis of the aortic valve. The coronary arteries were free and smooth.

The liver showed the typical nutmeg markings of chronic passive congestion. The pancreas was negative except that in scattered places there were minute areas of fat necrosis. The spleen showed chronic passive congestion. The spleen and liver presented a few fibrous adhesions to the diaphragm.

Cultures from the heart, liver, and spleen gave typical growths of the streptococcus. The one from the lower lobe of the lung yielded streptococci, staphylococci, pneumococci, and bacteria, rather complete bacteriology of the condition.

A PHYSICIAN: What was the mass in the left back?

DR. CABOT: Did you feel anything on the outside of the patient's back at necropsy?

DR. RICHARDSON: No.

DR. CABOT: I suppose we shall have to say it was fatty tumor.

DR. W. D. SMITH: Dr. Walker has just asked a very apt question, whether it is common, whether we expect a syphilitic aorta case to die with these marked signs of chronic passive congestion,—if that is the usual method of death.

DR. CABOT: In syphilitic aortitis with aortic regurgitation, if the aortic valve is involved, I should say yes, with chronic passive congestion. My impression is that that is the usual method of death, and that death with angina is less

common. Death from the results of aneurism, such as rupture, are less common still. Usually they die with passive congestion. Did you have a different impression?

DR. WALKER: I had an idea they did not die of chronic passive congestion so often as mitral.

DR. CABOT: I think as compared with mitral disease that is true. But taking one hundred deaths from syphilitic aortitis, to what will the majority be due? The majority will be congestive. But I do not think the per cent. of such deaths will be so large as in mitral stenosis. I have the figures on this, but I cannot remember them at this moment.

CASE 11253

ORTHOPEDIC DEPARTMENT

An Irish-American chauffeur of thirty entered October 31, 1918. His history before the present illness was not remarkable. For five years he had had pains with periods of remission in the spine, referred mostly to the thighs and abdomen. A knuckle appeared on his spine.

No general examination was made. The lower thoracic and upper lumbar spine showed a kyphos involving the fourth and fifth vertebrae. One or two vertebrae above this was another small sharp knuckle. The motions of the spine were limited to a few degrees. The knee-jerks were increased on the left. X-ray (see Plate I) showed rather extensive destruction of the first and second dorsal (?) vertebrae and of the intervertebral discs between them. To the right of the affected vertebrae was a large irregular shadow which was thought probably to represent an abscess.

A plaster jacket was applied. November 1 he was discharged.

January 13, 1919, he came in for fitting of a leather jacket. He was badly run down, weighing only 92 pounds. It was thought advisable to operate on him. His legs showed some spasticity. He was placed on a Bradford frame. The spasticity did not clear up from the left leg, and there were areas of anesthesia and paresthesia over the hip and leg. The jacket was fitted. January 26 he was discharged.

He remained in bed wearing the leather jacket night and day until April 26. Then he reported to the Out-Patient Department weighing 154 pounds. He was recommended to the wards for operation. At the time of his readmission, July 9, he weighed only 145 pounds, but felt very well.

Examination showed the point of maximum impulse of the heart 7 cm. to the left of the midsternal line in the fifth space, the left border of dullness 9 cm. to the left in the fourth space, the right border 2 cm. to the right.

The substernal dullness was not increased. A systolic thrill was palpable at the apex, where a soft blowing systolic murmur was heard. The rest of the examination was negative except for the kyphosis at the level of the first and second lumbar vertebrae covered with reddened skin, and a second smaller kyphosis at the level of the ninth and tenth thoracic vertebrae. There was no tenderness over either deformity or evidence of abscess under the skin. There was slight lumbar scoliosis with convexity to the right and a compensatory scoliosis in the thoracic region to the left. The movements of the spine were very limited, the spine being moved as a whole up to the level of the fourth or fifth thoracic vertebra. The lateral motions were likewise markedly limited, some motion occurring in the lower lumbar segments. There was no pain on forward bending and no costovertebral tenderness.

July 14 operation was done. The spinous processes were split longitudinally and an exogenous beef bone graft was placed in between the split surfaces, extending from the eighth dorsal to the fourth lumbar spinous processes. The periosteum was sewed together to hold the graft in place. The patient showed remarkably little reaction and had no pain. The wound healed well. The patient gained weight and looked much better than at admission. By the middle of August the site of the old kyphosis had become gradually smaller and was noticeably less sharply angulated. At his discharge August 30 he walked without pain, unsteadiness, or undue fatigue.

After leaving the hospital he was in bed seven weeks. After being up in his leather jacket two weeks he again started his work of driving a motor truck and lifting heavy weights. September 15, 1920, he felt a catch in his back while lifting a stove. He continued working for a week. Then his legs became numb and weak and he went to bed in his leather jacket. He suffered with severe girdle pains for three days and nights. He was then given a plaster jacket in the Out-Patient Department. The pains disappeared. Three months later, five weeks before his readmission to the hospital, the plaster jacket was removed and the leather jacket resumed. He had been in bed since September, 1920.

Examination at his readmission, February 9, 1921, was negative except for the neurological findings. He was not allowed to stand up because of weakness of his legs. The knee-jerks were exaggerated, equal. There was bilateral clonus and a suggestion of a Babinski on the left. Sensation was present on both sides, less acute in the entire left leg and abdomen.

A plaster shell was made, in which he was comfortable. February 17 exploration under gas and ether showed that the beef rib, which originally had a cancellous layer between each two cortical layers, was a solid piece of whitish

bone which seemed to have very small bleeding points. The graft was fused to all the spines except the fourth below the crack (see

processes was now done, and pieces of the flared spines put in to fill the gaps between the laminae and the spinous processes. A speci-

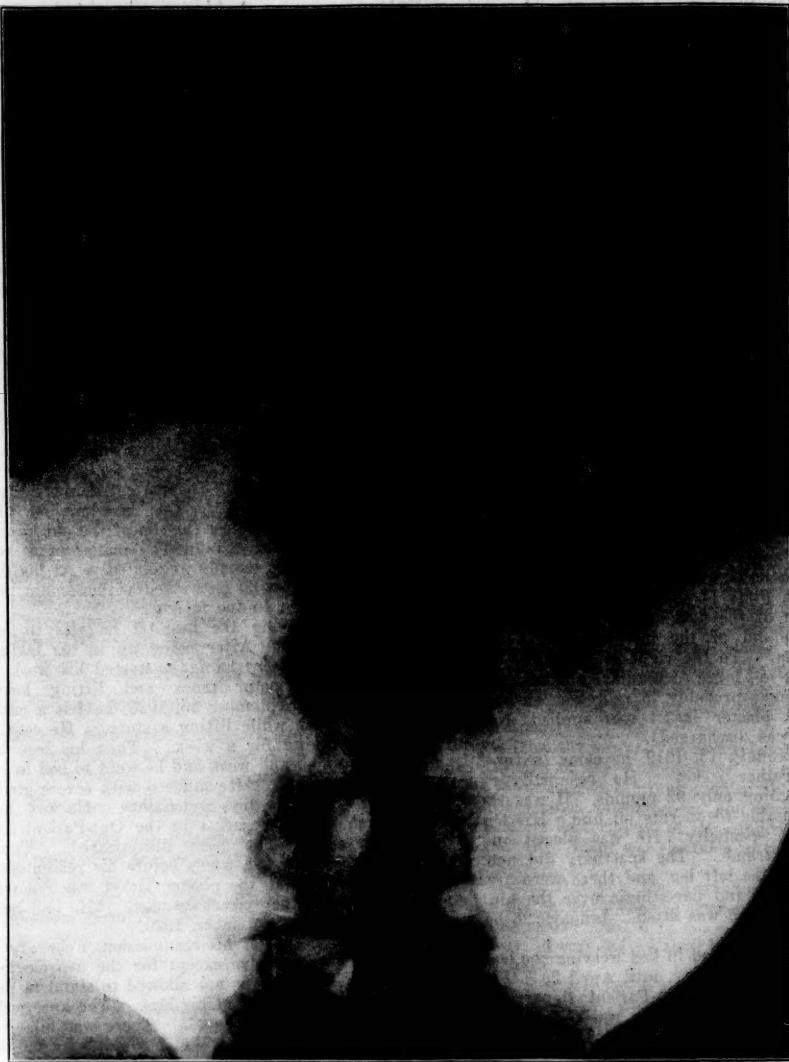


PLATE I. March 11, 1918. Shows rather extensive destruction of the first and second dorsal (?) vertebrae and of the intervertebral discs between them. To the right of the affected vertebrae is a large irregular shadow which was thought probably to represent an abscess.

Figure 1). The spinous processes were flared outward (see Figure 2), and the graft stood up in the middle. Fusion of the third, fourth and fifth spines on both sides of the spinous

men was taken for microscopical examination. It showed active proliferation of bone which was apparently extending into degenerate cortical bone. The patient made an uneventful

convalescence except for a phlebitis of the left leg. April 6 he was discharged.

He used the plaster shell for four months, then began to wear the leather jacket. With the exception of seven weeks during which he occasionally walked he was recumbent all the time. His condition was stationary. April 24, 1922, he returned to the hospital.

Examination was negative except for the spine and legs. There was slight bulging in the region of the eighth, ninth and tenth dorsal

vertebrae of the sixth, seventh, eighth and ninth being splintered, detached, and laid in the wound to overlap. The articular facets were everted. Osteoplastic shavings were cut off the laminae to fill in the spaces between the laminae. The post-operative treatment was a plaster shell.

The patient improved remarkably fast. May 4 he could move his legs and toes normally. June 8 another cistern-lumbar puncture showed both by dynamic and chemical tests a diminution of the severity of the block. The patient was clinically much improved, though he still showed evidence of pyramidal tract involvement (bilateral clonus). At his discharge June 11, 1922, the incision had healed and his general health seemed good.

DISCUSSION

BY DR. LLOYD T. BROWN

This case was selected because it brings out certain important points in the treatment of bone tuberculosis.

In the history the remissions of pain referred to the abdomen and legs for five years is interesting and not uncommon. This brings out the necessity of examining the spine in cases with such a history, where the local abdominal examination is negative.

After the diagnosis of tuberculosis of the spine was made ambulatory treatment in a plaster jacket was attempted and was a marked failure, so that from November to January the patient became very much run down and had signs of paraplegia of the legs. This shows the necessity of beginning recumbent treatment in these cases as soon as the diagnosis of active disease is made. By means of recumbency the man gained markedly in general condition, making the next step possible. This was an operative procedure to stiffen the spine in the diseased area, including two vertebrae above and below the disease. In this case an exogenous graft made from a boiled beef rib was used. After the operation the patient was allowed up on his feet in about six and a half weeks, at which time he showed no signs of paraplegia. In about three or four months after his operation he went back to his original heavy lifting work, with a gradual return of his paraplegia. The immediate cause of his return to the hospital was sharp pain in his back after lifting a heavy stove. Examination at this time showed a fracture of the graft where it had been put into the fourth lumbar spinous process. For this reason the second operation was done in February, 1921. From this time until April, 1922, he was recumbent all the time with the exception of seven weeks when he did a little walking. This was necessary because of the paraplegia. The third operation was done at this time, the beef bone graft removed and a fusion operation done including

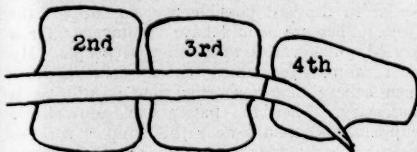


FIGURE 1.

vertebrae. Both legs showed marked loss of tonicity and complete loss of motor power. The abdominal reflexes were absent, the cremasterics very weak. The knee-jerks were hyperactive.

Graft fused to spinous process.

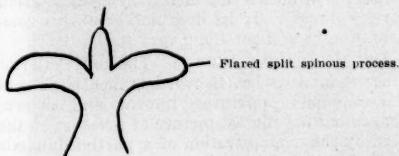


FIGURE 2.

Ankle clonus, patellar clonus and Gordon were present on the left, absent on the right. There was bilateral Babinski and Oppenheim. There was distinct evidence of diminished protopathic sensibility. Muscle sense was decidedly disturbed. He called his "up toe" down. A cistern-lumbar puncture showed well marked but not complete spinal subarachnoid block. Wassermann on the fluids was negative.

April 29 operation was done. The beef bone splint was found to be firmly fused to the tenth and eleventh dorsals. These spinous processes were also fused together. The beef splint from the eleventh dorsal to the first lumbar showed the outer cortex loose but the inner cortex apparently firm. The spinous processes were flared outward. There was a suggestion of movement between the eleventh and twelfth dorsals and the first and second lumbar. There was very definite fusion everywhere else in the old operative regions. The second and third lumbar were explored and seemed fused. All the beef bone splint was removed for examination. A complete fusion was now done, from the sixth to the third lumbar, the spinous pro-

both the diseased areas and two healthy vertebrae above and below. As can be seen from the history the patient from this time made great improvement and is at present able to be up and about without pain.

This case emphasizes very strongly the following points. The first one has already been mentioned, namely a physical examination which includes the spine as well as the abdomen in cases of obscure abdominal pain.

Second: If there is tuberculosis of the spine there is practically always tuberculosis somewhere else. In a series of some thirty cases fifty per cent showed at least two tuberculous foci present, one in the spine and a second in the lungs or elsewhere. In many of these cases a thorough search for the second focus had never been made.

Third: If a focus is found in one part of the spine be sure to get a complete X-ray study of the whole spine. In a series of thirty cases six showed second focus in the spine which was not always found at the first examination.

Fourth: The importance of recumbency cannot be overestimated in acute cases, especially where there are signs of paraplegia. Recumbency should be continued until the paraplegia disappears or by increasing makes operative exploration advisable.

DR. CABOT: Have you known other cases who had had paralysis so long and recovered?

DR. BROWN: I knew one case in which there had been paralysis for four years that got back the use of her legs so that she could walk. It requires recumbency, not being just laid down on the back but being put to bed in such a way that not only is the spine held in extension but the ribs are held upward and forward so that the diaphragm and the abdominal viscera can work to the best advantage. Personally I believe this can best be accomplished by means of a carefully fitted plaster shell.

Fifth: It is an interesting fact and one which played a very important part in the treatment of this case, as it does always in chronic cases, that this man was able, although recumbent, to learn a new trade. The result of this is that, as the man said, he need never go back to his heavy lifting job because he now can earn more in a job better suited for his present physical condition.

Sixth: It is necessary to point out that the treatment of tuberculosis of the spine in adults and children is very different. It is the consensus of opinion both abroad and in this country that in children operative procedures are in general not satisfactory. It is the feeling of those seeing these cases that in children recumbency for at least two years is necessary whether an operation is done or not. If at the end of this time we have no symptoms and the X-rays show increasing lime salt deposits we may allow the child to begin ambulatory treatment, but it

should wear carefully fitted supports and this support should be continued for about three years more.

In the adult we have a different situation. For social and economic reasons, except in the extremely well-to-do, such prolonged recumbency is impossible. It is therefore possible and advisable, if everything else is all right, to do some form of stabilizing operation on the spine. By doing this we are putting a splint into the back, and that is all. We are not doing anything at all to the disease, but simply putting in a splint in the best possible way to support the back. Then we should have recumbency for a period which varies with different people. My own feeling is recumbency for six months. Other men believe that a shorter time is all that is necessary. Then the patient gets up with a support, and should wear this support for two years anyway. If this is done we can feel pretty sure that the patient will get along unless he does things which will tire him out. If he gets overtired and if he goes beyond his ability, since he has tuberculosis in him he breaks his compensation for his disease and is going to get into trouble again. Therefore a man who once has had tuberculosis of the spine must always remember that he is living merely by compensation for his disease. If he does not break his compensation he will get along very well.

DR. F. FREMONT-SMITH: The only interest other than what Dr. Brown has mentioned was the combined punctures, lumbar and cistern, confirming the clinical picture of pressure on the cord by the demonstration of a partial dynamic block between the lumbar and cistern fluids as shown by manometer differences, and also by the increased protein in the lumbar fluid. The second puncture, after operation, showed that this block had been largely relieved.

DR. BROWN: How soon after the operation was the second puncture made?

MISS PAINTER: It was on June 8. Operation was April 29.

DR. BROWN: There is a question as to what causes the paralysis in one of these tuberculous spines. We may get it from all sorts of things. We may get it from what I suppose we should call edema, a swelling around the disease, which works its way back into the spinal canal. We may get it from a cold abscess breaking into the spinal canal. And we had one very interesting case showing that we may get it from still other things. This was a boy who many years previously had a tuberculous hip disease, but who for years had been perfectly well. Suddenly he began to have back pain, very extreme, with the formation of a knuckle, and extreme spastic paraplegia. Finally it was necessary to do a laminectomy; at which time there was found directly underneath the kyphosis an area of granulation tissue. This was evidently getting bigger and bigger and the boy was getting

worse. After the relief of pressure by the operation he began to recover from his paralysis and his pain began to get less. I have also heard of a case where there was just an area of fat that had got in under the kyphosis, causing pressure.

DIAGNOSIS

Tuberculosis of dorsal and lumbar spine.

LATER NOTES

At home his legs improved a great deal until August, 1922, when he began to stand. After

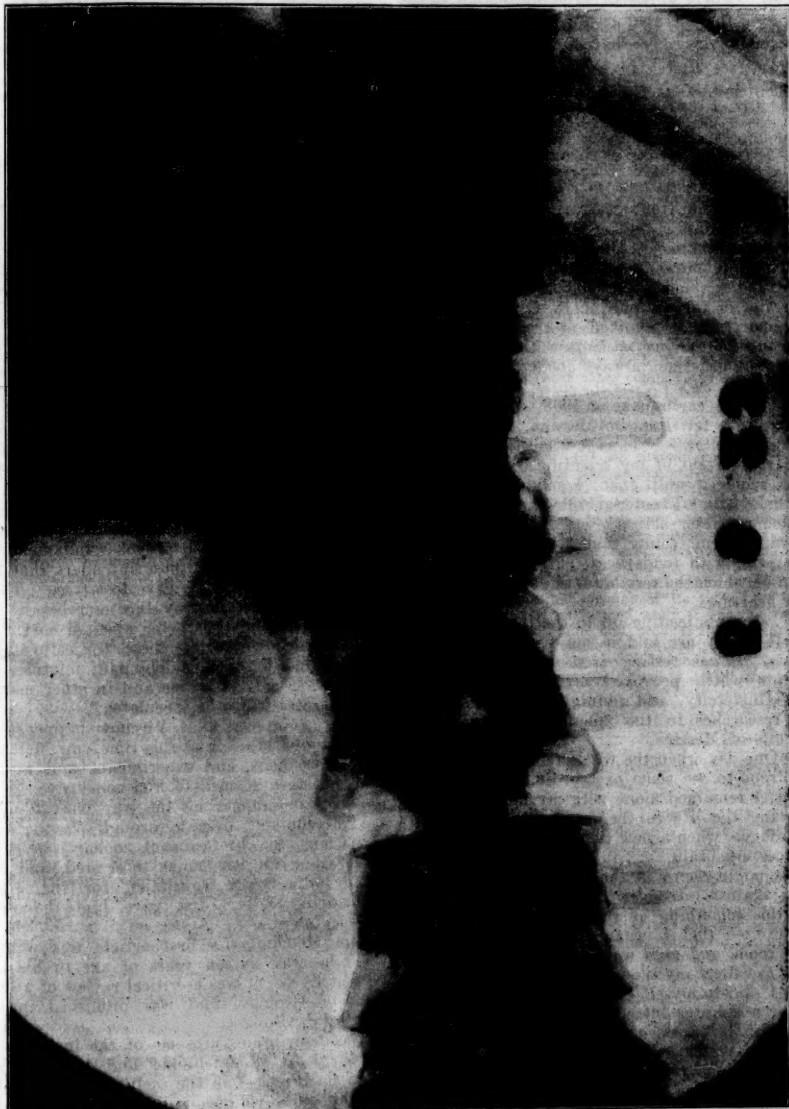


PLATE II. May 9, 1923. Shows the appearances much as before. The bone grafts are not visible.

three days his legs gave out entirely and he remained recumbent. May 9, 1923, when he reported at the Out-Patient Department, more normal feeling was coming back and he could move his legs fairly well. Examination showed sustained ankle clonus and lively knee-jerks. There appeared to be no motion in the spine in the operated area. There was a slightly tender spot in the middle of that area. X-ray (see Plate II) showed the appearances

much as before. The bone grafts were not visible.

Records of the Social Service Department show that in May, 1924, the patient had regained almost the entire use of his legs. Dr. Brown found the spine in most satisfactory condition. In December the patient was seen at home, convalescent from an operation for ulcers of the stomach. He was able to stand and walk easily and had good control of his legs. He was doing very light work.

MEDICAL HISTORY

THE INCEPTION OF THE PHAGOCYTE THEORY

How Metchnikoff came to evolve the theory of phagocytosis is told in Madame Metchnikoff's delightful volume, "Life of Elie Metchnikoff." Wishing to pursue researches on the shores of the Mediterranean, the Metchnikoffs settled at Messina in the autumn of 1882. It was only necessary for Metchnikoff to cross the quay to obtain the marine specimens that he wished from the fishermen always about the quays and beaches.

After the earthquake of 1908 we are told that he wrote a few lines on Messina, the final ones being as follows—"Thus it was in Messina that the great event of my scientific life took place.

A zoologist until then, I suddenly became a pathologist. I entered into a new road in which my later activity was to be exerted. It is with warm feeling that I evoke that distant past and with tenderness that I think of Messina of which the terrible fate has deeply moved my heart."

The events leading up to the inception of his great theory are told in his own words as follows, "I was resting from the shock of the events which provoked my resignation from the University, and indulging enthusiastically in researches in the splendid setting of the Straits of Messina.

"One day when the whole family had gone to a circus to see some extraordinary performing apes, I remained alone with my microscope, observing the life in the mobile cells of a star-fish larva, when a new thought suddenly flashed across my brain. It struck me that similar cells might serve in the defense of the organism against intruders. Feeling that there was in this something of surpassing interest I felt so excited that I began striding up and down the room, and even went to the seashore in order to collect my thoughts.

"I said to myself that, if my supposition was true, a splinter introduced into the body of a star-fish larva, devoid of blood vessels or of a nervous system, should soon be surrounded by mobile mesodermic cells have to strive. These runs a splinter into his finger. This was no sooner said than done. There was a small gar-

den to our dwelling, in which we had a few days previously organized a 'Christmas Tree' for the children, on a little tangerine tree; I fetched from it a few rose thorns and introduced them at once under the skin of some beautiful star-fish larva as transparent as water.

"I was too excited to sleep that night in the expectation of the result of my experiment, and very early the next morning I ascertained that it had fully succeeded.

"That experiment formed the basis of the phagocyte theory to the development of which I devoted the next twenty-five years of my life."

Madame Metchnikoff tells us that Metchnikoff reasoned as follows: "In man microbes are usually the cause which provokes inflammation, therefore it is against those intruders that the mobile mesodermic cells have to strive. These mobile cells must destroy the microbes by digesting them and thus bring about a cure."

"In order to verify these conjectures, he started studying the englobing of microbes by mesodermic cells in larvae and in other marine invertebrates which he inoculated."

It is of interest that Virchow happened to pass through Messina at this time, saw Metchnikoff's specimens, and experiments, and we are told that they seemed to him conclusive.

The next summer on the way back to Russia, Metchnikoff passed through Vienna and saw Claus, the professor of zoology; he, with other scientists, was much interested, and was asked for a Greek translation for the words "devouring cells," and gave him the word *phagocytes*.

Elie Metchnikoff's first article was written when he was sixteen years of age in his last year at Lycee; it was a critical review of a textbook of Geology, and was published in the *Journal de Moscou*.

The descriptions of some of the incidents in the early life of Metchnikoff and "Country life in Little Russia," in the early part of Madame Metchnikoff's volume, will prove a delight to those who do not know the work.

CURRENT LITERATURE

ABSTRACTORS

GERARDO M. BALBONI	TRACY MALLORY
WILLIAM B. BREED	HERMAN A. OSGOOD
LAURENCE D. CHAPIN	FRANCIS W. PALFREY
AUSTIN W. CHEEVER	EDWARD H. RISLEY
RANDALL CLIFFORD	GEORGE C. SHATTUCK
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CHARLES D. LAWRENCE	SHEIELDS WARREN
BRYANT D. WETHERELL	

IODINE AS AN AID TO SURGERY IN THE TREATMENT OF EXOPHTHALMIC GOITER

JACKSON, A. S. (*The Lancet*, Apr. 11, 1925), discusses at length iodine as an aid in the treatment of exophthalmic goiter. He finds that "the use of iodine, as advocated by Plummer in the treatment of exophthalmic goiter, is the most important factor in reducing the operative mortality in this series."

"The development of a highly perfected operation, with the consequent reduction in time, the fact that patients come to operation at an early stage in the disease, and improved methods of anesthesia, are other factors tending to reduce the operative mortality."

"Iodine will not permanently cure, but merely temporarily alleviate the symptoms of exophthalmic goiter.

"The use of iodine will prevent or terminate a fatal crisis as well as postoperative hyperthyroidism.

"The necessity for ligation is eliminated in 90 per cent. of cases by the use of iodine.

"Patients are given 30 drops of Lugol's solution daily for three days and 40 or 50 drops for one or two days. Following operation Lugol's solution is administered by mouth and by proctoclysis.

"The average stay in the hospital is reduced to five days, as the patients are able to take the preoperative treatment at home.

"Within 48 hours after the ingestion of iodine there is a marked abatement of all the symptoms of hyperthyroidism. The nervous, vascular and digestive systems are all favorably influenced."

[R. C.]

THE PREVENTION OF Puerperal Morbidity AND Mortality

IVENS, FRANCES (*Brit. Med. Jour.*, Mar. 28, 1925), is of the opinion that latent or preexisting infection, streptococcal, gonorrhoeal, or coliform, is responsible for a considerable percentage of cases of puerperal sepsis; that the organism may not infrequently be isolated by bacteriological examination of the urine during pregnancy, especially in cases of streptococcal or coliform infection; that intermittent albuminuria during pregnancy is an indication for a bacteriological examination of the urine, even in the absence of urinary symptoms.

[R. C.]

PYLOROSPASM AND CEREBELLAR TUMOR

PORGES, from Wenckebach's clinic at Vienna, reports (*Wien. klin. Woch.*, February 5, 1925) a case of pylorospasm in an adult with a cerebellar tumor with pressure on the dorsal vagus nucleus. This is of interest with reference to the etiology of pylorospasm in infants.

[R. M. G.]

MOVABLE KIDNEY

MATHE, C. P. (*Surg., Gyn. and Obst.*, May, 1925), revives the old-time discussion in regard to operation for movable kidney and believes that the operation has fallen into disrepute because unsuitable cases were subjected to operation when some other condition might possibly have been the cause of the symptoms. He states that in order to properly select cases more thorough diagnostic methods than have been used in the past should be employed. Those cases which by pyelogram show kinking of the ureter are ideal for operative treatment. The article contains many X-ray illustrations of the author's text. He states in conclusion that the condition is more common in the female because the renal fossae are shallower, cylindrical or even funnel shaped, being wider below than above. This predisposition to displacement is increased at puberty because of the widening of the bony pelvis. In males the renal fossae are pear-shaped, being narrower below. Its greater frequency on the right side is due to the shape of the renal fossa, the presence of the liver on that side, and the weaker support afforded by the less well developed right perirenal fascia. The majority of cases of renal ptosis can be relieved by the proper abdominal support, fattenning, and strengthening exercises. Nephropexy is a justifiable operation. It has been employed by numerous urologists of note who have found it satisfactory. It relieves symptoms and is indicated in the following cases of movable kidney: (a) when the belt fails or is poorly tolerated; (b) in those cases complicated by ureteral kink caused by fibrous bands; (c) when the sag of the kidney has caused the ureter to kink over an aberrant vessel; (d) in those cases in which adhesions have developed around a prolapsed kidney, holding it in place; (e) in chronic colon pyelitis when faulty drainage due to increased mobility is not corrected by the belt. We have employed nephropexy with success in 96 per cent. of the 30 cases operated on. Of those, 46 per cent. had obtained no relief from mechanical supports although they had been employed for some time, varying from six months to one year. A review of the literature leads us to believe that surgical suspension has fallen into disrepute, but not on account of its inefficacy, but because it has been performed when it has not been indicated, the technique has been faulty, or there has been failure to realize the necessity of exposing the ureter and relieving any condition which might be present, which, unrelieved, would defeat the purpose of the operation.

[E. H. R.]

OCCUPATIONAL AND OTHER CAUSES OF PULMONARY FIBROSIS

OLIVER, T. (*Brit. Med. Jour.*, Apr. 11, 1925), in a most interesting article, finds as a result of pathological research that particles of silica which are below two microns are the most dangerous, so that while a man may be working in a thick atmosphere heavily laden with dust, readily visible to the naked eye, yet if most of these particles are above, say, 50 microns, there is less likelihood of this dust causing silicosis than an atmosphere in which the particles are smaller than 2 microns in dimension.

[R. C.]

WASSERMANN REACTION IN PROSTITUTES

KLEMM of Leipzig (*Münch. med. Woch.*, December 12, 1924) finds that 33 per cent. of all prostitutes present a positive Wassermann reaction without further evidence of syphilis.

[R. M. G.]

GLIOMA OF THE BRAIN

SACHS, ERNEST (*Ann. of Surg.*, May, 1925), discusses the surgical aspects of glioma of the brain and draws the following conclusions:

"All gliomas that are cystic in character, or, if solid, have a sharp line of demarcation, are composed of glial nuclei, are favorable cases for radical removal, and these cases, especially the cystic variety, offer a very good prognosis. Those that are deep-seated in the cerebellum are less favorable, but are so soft that, with suitable suction apparatus, they can probably be quite completely removed by that method, but they show a great tendency to recur. I have hoped that by the proper application of the suction method some of these solid tumors might be transformed into cysts, so that at a subsequent operation one might have a cyst to deal with, which would simplify the problem. As yet I have not had an opportunity in which to determine whether this can be done. Deep-seated tumors in the cerebrum are infiltrating tumors, and are unfavorable cases to deal with. One never knows if one has removed them in toto, for the transition from normal to abnormal tissue is often imperceptible. These are the rapidly growing tumors and have a bad prognosis. There are some gliomas that seem to respond to deep X-ray therapy. I have a few such cases under observation, but I do not know whether the cases that respond to X-ray all belong to one of these histological groups or to different ones. Whether this method of studying gliomas will prove useful time alone can tell. It may be that the employment of these new staining methods will give us a sounder basis of classification. The principle, however, remains the same: to try to correlate our histological findings with the clinical pictures and thus establish sounder bases for treatment than we have had in the past."

[E. H. R.]

THE SUBSTITUTION OF THE ERECTOR SPINAEE FOR PARALYZED GLUTEAL MUSCLES

KREUZSCHER, P. H. (*Surg., Gyn. and Obst.*, May, 1925), describes a new operation for stabilizing the hip in cases where the gluteal muscles are paralyzed. The article contains some beautiful drawings of the operative procedure. The advantages of this operation are the following:

1. It permits us to conform with the long-established rule, namely, that in transplantation of tendons or the use of silk sutures the traction must be in a direct line with the tendon or bone to which they are attached.
2. This muscle acts synergistically with the gluteal muscles for which it is used as a substitute.
3. Easily one-half of the volume of this muscle can be utilized without interfering with the normal erector spinae action.
4. By dividing the muscle as described above, one does not noticeably interfere with the blood supply of the loosened portion. There is very little bleeding from the muscle tissue itself when it is detached.
5. We were able to restore complete stability of the hip-joint in a totally paralyzed extremity.
6. By the use of the erector spinae muscle we were able to produce very definite gluteal action.
7. With a stable hip and gluteal action the patient is able to walk about unaided.

[E. H. R.]

GAS CYSTS OF THE INTESTINE

MILLS, H. W. (*Surg., Gyn. and Obst.*, Mch., 1925), presents a very interesting paper, beautifully and adequately illustrated, on this very unusual subject, and gives an excellent bibliography. The article is of considerable interest.

[E. H. R.]

GYNECOLOGICAL CONDITIONS TREATED WITH RADIUM ALONE OR COMBINED WITH SURGERY

SMITH, W. S. (*Surg., Gyn. and Obst.*, May, 1925), presents an article discussing the results in 156 cases in the treatment of such conditions as chronic metritis, fibroids, carcinoma of the cervix, adenocarcinoma of the corpus uteri, and states that his impressions are as follows:

1. Radium, heavily screened with one millimeter of platinum and two millimeters of rubber and used within the uterus in 1200 to 2400 milligram hour doses, even with repeated administrations, causes no untoward effect on bladder and rectum and produces very little troublesome leucorrhœa. If the radium is used within the vagina without careful protection of bladder and rectum it will cause a reaction; but not nearly so disastrous as would be the case if B-rays were used.
2. The temperature reactions occasionally seen are more likely to be due to a fresh invasion by organisms started by the curetting and blocked drainage than radium.
3. Radium alone is an excellent treatment for chronic metritis and small fibroids at the menopause age, curing most of the cases with one 1200 milligram hour dose; but even a 2400 milligram hour dose will not always control the bleeding indefinitely in all patients.
4. Plastic operations on cervix and perineum may be performed with excellent results at the same time that radium is applied to the interior of the uterus.
5. For advanced cases of cancer of the cervix and corpus, radium, as a palliative measure, gives more relief than any other treatment at our command.
6. In early cervical cancers, the Byrne cauterization, and radium at the same session, with or without X-ray treatment later, give results which are so valuable that it should be thoughtfully considered as a possible standard method of treatment.
7. It is impossible to forecast how much or how little radium treatment will accomplish for any particular patient suffering from carcinoma.

[E. H. R.]

AN INVESTIGATION INTO THE ETIOLOGY OF PUERPERAL FEVER

BIGGER, J. W., and FITZGIBBON, G. (*Brit. Med. Jour.*, April 25, 1925), are of the opinion that:

1. The commonest form of puerperal sepsis, that caused by haemolytic streptococci (and particularly Strep. pyogenes), is due to exogenous infection.
2. Non-haemolytic streptococci do occasionally cause puerperal sepsis. These organisms are present in the vagina of the majority of parturient women and are found fairly frequently in the uterus post partum. The cause of the puerperal sepsis is the streptococci of the vagina plus some unknown factor, which may be a local or general lowering of the patient's resistance or a rapidly enhanced virulence of the organism.

[R. C.]

SEXUAL DEVELOPMENT AND OTOSCLEROSIS

STEIN of Innsbrück presents (*Wien. klin. Woch.*, January 22 and 29, 1925) his series of studies on stages of sexual development in their influence on otosclerosis, to which he believes they bear a definite causal relation.

[R. M. G.]

RATE OF ABSORPTION OF FLUIDS BY DIFFERENT ROUTES

UNDERHILL and WEINSTEIN (*Jour. Metab. Res.*, November-December, 1923) noted no difference in the rate, by mouth, subcutaneously or intraperitoneally.

[H. G.]

AMERICAN JOURNAL OF PATHOLOGY, MARCH, 1925

BOYD, G. L., and ROBINSON, W. L., present the clinical and autopsy findings in a case of diabetes which had been treated with insulin. The 9-year-old boy had been recognized as a diabetic at the age of 2 and did fairly well on an Allen diet. When insulin treatment was begun he weighed 30 pounds and had a carbohydrate tolerance of less than 15 grams. A year later, when his weight had increased over 50 per cent, and his insulin requirement had dropped to one third of the original amount, he was killed while coasting. At autopsy the islands of Langerhans showed definite evidences of regeneration. Not the least valuable portion of the article is the discussion of pancreatic regeneration, by Dr. Bensley.

MELENBY, E. E., gives a detailed study of kala-azar, particularly of the tissue reactions to the parasite. The important role of the endothelial leucocyte in this disease is emphasized. A number of excellent figures illustrate the various points brought out in the text.

PEABODY, F. W., and BROWN, G. O., emphasize the importance of phagocytosis of erythrocytes in the bone marrow, particularly in cases of pernicious anemia. While phagocytosis of red cells by endothelial leucocytes of the bone marrow occurs to a slight degree normally, and is readily noted in pneumonia, typhoid fever and other infectious conditions, it is very marked in cases of pernicious anemia which died in an acute stage of the disease. The authors suggest that this phagocytosis may be a factor in the hemolytic jaundice and anemia present in the disease.

A thorough clinical and pathology study of 35 cases of acromegaly is presented by BAILEY, P., and DAVINOFF, L. M. The illustrations are excellent and of great value to students of the subject, and the careful histories will be a material aid to early diagnosis of this fortunately rare condition. The essential lesion they feel to be an adenoma consisting of cells with "a" granules, located in the pars distalis. A careful analysis of the literature shows the few cases of acromegaly supposedly with other types of lesion in the hypophysis to have been erroneously interpreted or inadequately studied.

The etiology of acute appendicitis is still in dispute, some claiming a specific causal agent and others a variety of them. WARREN, S., reports the result of a study by combined bacteriological and pathological methods. *B. coli* was found alone in 25 acutely inflamed appendices, and with other organisms in 12. *Streptococcus hemolyticus* occurred alone in 6 and combined with colon bacilli in 9. *Proteus vulgaris* and *B. pyocyanus* were each found 5 times. Other organisms encountered were *Streptococcus viridans*, non-hemolytic streptococcus, and *Pneumococcus type I*. In one case of acute periappendicitis in a woman with pelvic inflammation, the gonococcus was recovered from the appendix. The infection is probably from the lumen, except in the cases where there is extension from the pelvis. The activity of the musculature is important in preventing stasis of the contents of the lumen and accumulation of poisonous bacterial products. Acute appendicitis is not a specific disease due to one type of organism, but, like acute endocarditis, acute tonsillitis and certain other lesions, may be caused by a variety of organisms. Two cases are reported in which acute appendicitis occurred without symptoms.

[S. W.]

CORRELATION OF THE ENDOCRINE GLANDS

MENDEL, from Goldscheider's clinic at Berlin, presents (*Münch. med. Woch.*, February 6, 1925) a new and interesting diagrammatic study of correlation of the endocrine glands.

[R. M. G.]

SURGICAL COMPLICATIONS OF DIABETES UNDER INSULIN TREATMENT

GAGER, L. T. (*Surg., Gyn. and Obst.*, May, 1925) very concisely discusses the rationale of treatment of surgical cases, especially those complicated by infection, gives the case histories of eight cases to the point, and draws the following conclusions: "By the use of properly balanced and restricted diets and adequate doses of insulin, carbohydrate combustion sufficient to prevent acidosis may be maintained. Similarly, the level of the blood sugar may be kept low, thus providing an essential basis of satisfactory wound healing. In general, infections should be given the benefit of early operation, from the standpoint of the diabetes as much as from that of the surgical condition.

"The welfare of the diabetic patient requiring surgical operation demands respect for the principles of metabolism in diabetes and the methods of their application."

[E. H. R.]

JUVENILE PARESIS

ROSENHECK, C. (*Am. Jour. of Syph.*, 9:96, Jan. 1925), presents in detail two case histories and states that juvenile general paralysis is the product of a prolific and degenerate stock plus a congenitally acquired syphilis. The clinical picture of general paralysis in childhood or youth is rarely as typical as that of the adult. This is obviously due to the incomplete cerebral development and insufficient mental acquisitions. In the main, however, the symptomatology differs very little from the adult form. Two marked features are, however, present in the juvenile form which are worthy of mention. These are entire absence of grandiose ideas and early and progressive deterioration.

[A. W. C.]

THE DICK TEST IN SCARLET FEVER

OKELL, C. C., and PARISH, H. J. (*The Lancet*, Apr. 4, 1925), give the following conclusions:

1. Amongst 95 medical students 74 per cent gave positive response to the Dick test. Amongst 20 who had a history of scarlet fever, 65 per cent gave a positive reaction; of 75 students who had no history of scarlet fever, 24 per cent were negative to the Dick test.

2. Amongst 120 patients entered in the hospital records as convalescent from scarlet fever, 82 per cent. gave a negative reaction; amongst the 22 (18 per cent.) with a positive reaction there were 6 giving a strongly positive reaction, who were considered to have had a definite attack of scarlet fever.

3. On the whole, our experience of the test agrees with that of Dick, Zingher and others.

[R. C.]

ON THE IDENTITY OF HAEMATOIDIN AND BILIRUBIN

RICH, A. R., and BUMSTEAD, J. H. (*Bull. Johns Hopkins Hosp.*, Apr., 1925), support the belief that haematoidin and bilirubin are identical. They found that when haematoidin obtained from the haemorrhagic contents of a cyst of the omentum has been subjected to the physical and chemical tests and reactions which are characteristic of bilirubin, in every instance it has behaved precisely as did a control of pure bilirubin. In this study urobilin (hydrobilirubin) was prepared from haematoidin by reduction, and cholecyanin (bilicyanin) by oxidation. These are characteristic oxidation and reduction products of bilirubin.

These facts are offered in support of the belief that haematoidin and bilirubin are identical.

[R. C.]

THE BOSTON Medical and Surgical Journal

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The Massachusetts Medical Society

THE one hundred and forty-fourth anniversary of the founding of this Society was a notable occasion in the medical history of this state.

We were favored with good weather and large attendance. Six hundred and eight fellows registered and four hundred and eighty-five sat at the banquet at the Copley-Plaza in the evening.

The section meetings were well attended. The papers read were all interesting and, to use a common expression, very practical.

The Annual Oration by Dr. David Cheever which was published last week presented some of the problems and responsibilities which are of definite concern to the Society and should lead to action. About 350 were in attendance.

The Shattuck Lecture by Professor Zinsser was an exposition of the obtruse problems of immunology dealing first with the diseases caused by recognized microorganisms and then with those conditions resulting from invasion by a specific filterable virus. This recondite subject called for ingenuity in the presentation of present-day facts and theories in order to enable the untrained listeners to get a fair idea of the accomplishments of scientists. The

speaker succeeded admirably and showed how the research worker is bringing scientific data to bear on the work of the clinician and closing the gap between the two.

The audience numbered 250. Professor Zinsser's paper is published in this issue.

The Council Meeting was well attended and the reports of committees met with cordial approbation. When the resolution of the Middlesex East District Society relating to the limitations of the use of anaesthetics to physicians was presented, it was quite evident that many of those present preferred the somewhat common way of least resistance and freedom of action rather than the application of logic in facing a definite problem.

It is difficult to understand how any great proportion of the profession can be complacent in the presence of a question which presents a definite possibility of serious complication. The giving of anaesthetics is justly regarded as an important professional service. Either the nurse has a right to serve as an anaesthetist or she cannot under all circumstances assume the responsibilities of this form of professional activity. Differences of opinion relating to this subject exist and if there is any legal obstacle it should be removed if the profession wishes to endow her with this function. The problem presents ethical and economic questions and the report of the committee will be awaited with interest.

The formation of a section to study the questions relating to the status of physiotherapy and the apparatus employed by some practitioners is an important move and in line with efforts made elsewhere to provide the profession with a guide to ethical and efficient practice.

The Council unanimously elected the following named persons for the various offices for the year:

President—James Savage Stone.
Vice-President—Michael F. Fallon.
Secretary—Walter L. Burrage.
Treasurer—Arthur K. Stone.
Orator—Charles F. Painter.

Librarian Emeritus—Edwin H. Brigham.

The Committee of Arrangements had all the details of the meetings well in hand and the sessions began and ended on time. The courtesy of the John Hancock Life Insurance Company in providing the hall free of expense was recognized by a vote of thanks. This contribution enabled the committee to carry through the program well under the appropriation.

It is to be expected that there will be differences of opinion as to the best kind of a medical meeting, but it must be kept in mind that each succeeding Committee of Arrangements will try to provide a meeting which may be serviceable to the greatest possible number and accomplish the greatest amount of good. This last program proved especially attractive to out of town members. The relatively small

number of Suffolk District doctors was a definite disappointment.

It may not be out of place to suggest that a larger representation from Suffolk County would be gratifying and that these members could add much to meetings by mingling with the outside visitors and telling of the work done in the metropolitan center.

THE BANQUET

THE members and guests assembled in the banquet hall of the Copley Plaza at 6:40 and were welcomed by President Bigelow. After the bountiful repast had been disposed of the President called the meeting to order and presented the guests by name to the assembly and expressed regret that the Secretary, Dr. Burrage, was unable to be present.

He gave a brief resume of the activities of the Society and paid a tribute to the doctors of New England who are not only maintaining the high traditions of the profession but who are also in the foremost ranks of the Country's educators. In asking for continued service for the people he counselled the profession that although the mantle of the Society is wide, it should not cover the member who willfully violates the laws of the Commonwealth or who sits at ease indifferent to the cry of suffering and distress, and then introduced the speakers with appropriate references to the character and service which each represented.

Governor Fuller brought the greetings of the Commonwealth of Massachusetts to the Society, complimented the members for the service rendered to individuals and the State and assured the Society that he would coöperate in efforts to promote higher standards of medical education and practice.

Bishop Slattery responded to the sentiment that the meeting was honored by the presence of a great hearted man who loves God and his fellow-men. The Bishop brought out the importance of the influence of the clergy, physicians and teachers who together are working for the uplift of the race and who must coordinate in all the plans for the betterment of humanity and emphasized the opportunities and responsibilities of the general practitioner and the specialist, giving to each commendation for the great service rendered to mankind.

Sherman L. Whipple responded for the legal profession and, after announcing that he is the son of a country physician who practiced in a New Hampshire town, told in a humorous vein of the responsibility thrust upon his father who, as President of the State Society, prepared an address under the inspiration and assistance of his wife. He then took as the subject of his address "The Expert Witness," explaining the difficulties encountered by physicians who, not being familiar with the rules of evidence, were

unable to give full expression to their opinions before the courts. He explained the embarrassing situations in which intelligent people often find themselves when testifying, which are due to archaic rules established by precedent and which must be followed until legal procedure can be made more elastic and better fitted to meet the complexities of modern life. He paid tribute to the honesty of purpose of Mr. Goodwin in his efforts to secure safety for the people and at the same time defended the judges who are, he believed, always honest and loyal in their efforts to enforce law but who are helpless at times under our present judicial system.

Professor James J. Walsh of New York then gave his popular lecture on "The Cures That Fail," taking up the history of the useless drugs and mechanical devices which have been popular from earliest history down to the present time, and which were regarded as cures by thousands of people during periods of popularity but which are known to have been without any effect in curing disease except through the mistaken beliefs of those who testified to the benefits conferred.

The exercises were brought to close by the introduction of President James S. Stone, who appealed for the coöperation and assistance of the fellows in efforts which will be made to raise the standards of medical education.

This brief account will, we trust, lead to a careful study of the Secretary's official report of the Proceedings of the Society and the Council which will be published soon.

THE PRESIDENT OF THE MASSACHUSETTS MEDICAL SOCIETY

ELECTED BY THE COUNCIL JUNE 9, 1925

If precedent is to be followed, the affairs of this Society will be under the leadership of Dr. James Savage Stone for the next two years.

Dr. Stone was born in Newton August 21, 1868, the son of Dr. Lincoln B. and Harriet Hodges Stone. His father, now retired, and his mother are living in Newton. His father has practiced in Newton, all but a short time spent in the South, throughout his professional career.

Dr. James S. Stone graduated from the Newton High School in 1885, from Harvard College in 1889 and after one year with the Texas Geological Survey entered the Harvard Medical School, graduating in 1894. He served as Surgical House Officer in the Massachusetts General Hospital and in the Boston Lying-In Hospital. He has practiced in Boston since terminating these hospital appointments, serving on the staffs of the Boston Dispensary, the Infants' Hospital, the Children's Hospital, and for a short time on the staff of the Carney Hospital. He is now Visiting Surgeon at the Children's Hospital and is Consulting Surgeon at

the Boston Dispensary, the Boston Floating Hospital and the Framingham Hospital. During the war, he was surgeon at Base Hospital, Camp Jackson, 1917-1918, where he contracted meningitis and narrowly escaped death. He is a member of the American College of Surgeons, the New England Surgical Society and the Boston Surgical Society.

He has been prominent in local and state medical activities, has served as president of the Suffolk District Medical Society and for many years on the Committee on State and National Legislation and on very many other important committees of the parent society.

He has been intensely interested in Medical Education and all matters relating to ethical practice.

With this background of wide experience and with a spirit of consecration to medicine, the Society may confidently look forward to an era of progress under his administration.

AN X-RAY TIMER

A NEW instrument has been devised by Charles N. Weyl of the Moore school of electrical engineering of the University of Pennsylvania and has been used experimentally at the Phipps Institute of the University during the past year. Its object is to time the exposure of the film of the chest so that it will take place during a rest phase of both heart and diaphragm. By this means more clear cut impressions of heart and lung pathology are gained. The mechanism is so delicate that it will operate with stability when the motion of the diaphragm is as much as 1.5000 of an inch.

With the instrument in use the patient stands with his back to the tube and his chest against the film holder. A small funnel is placed over the carotid artery and is connected by a rubber tube to the "pulse relay" on a nearby table. With each pulse beat an impulse is sent down the connecting tube causing an exposure of the film.

It seems probable that this simple improvement in technique may increase considerably the accuracy and usefulness of chest roentgenography. We are all familiar with the discrepancies that may exist between heart shadows as filmed in systole or diastole, and the making of mediastinal conditions in the latter phase. Certainly with this new method there should at least be more accurate standards for comparison.

The Massachusetts Medical Society

MEMBERSHIP CHANGES

FROM MAY 1, 1925, TO JUNE 10, 1925

Official List Prepared by the Secretary

NOTE:—The deaths have appeared in the "Recent Deaths" column of the *Journal*. The changes made

by the Council, June 9, will be found in the "Proceedings of the Council," the names of new Fellows and deaths for the year in the "Proceedings of the Society" in the *Journal* on or before July 10, 1925.

Atkinson, Frederick C., North Andover, from 222 to 257 Main St.

Ayer, Silas H., from Brookline (Norfolk) to Boston (Suffolk), 318 Shawmut Ave.

Baehr, Frank H., from Boston (Suffolk) to Springfield (Hampden), 760 Summer Ave.

Baker, Lewis F., Fitchburg, now his address is Nichols Rd.

Barstow, Carl E., Arlington, from 1152 to 754 Massachusetts Ave.

Baxter, Raymond H., Marion, from Pleasant St. to 6 West St.

Bier, Max D., Lawrence, from 50 Concord St. to 46 Amesbury St.

Blankhorn, James, Stoneham, from 301 Main to 26 Maple St.

Brush, Joseph A., from Cambridge (Middlesex South) to Roxbury (Norfolk), 88 Francis St.

Buck, Robert W., Boston, has moved his office from 374 Marlborough St. to 475 Commonwealth Ave.

Burt, Edward W., Westport, office now New Bedford, 101 School St.

Burton, Oscar A., from Wellesley (Norfolk) to Sarasota Heights, Fla. (Non-Resident List).

Bush, Arthur D., from Emory University, Ga., to Decatur, Ga., 207 Clairmont Ave.

Cobb, Stanley, from Paris, France, to Oxford, Eng., 10 Lathbury Rd.

Consentino, A. B., Lawrence, from 7 Jackson Ct. to 64 Newbury St.

Cregg, Francis A., Lawrence, from 477 Essex St. to 46 Amesbury St.

Cregg, Herbert A., Lawrence, from 477 Essex St. to 46 Amesbury St.

Crosbie, Arthur H., from Boston (Suffolk) to Brookline (Norfolk), office Boston, 520 Commonwealth Ave.

De Cicco, Luigi, Fitchburg, from 381 to 353 Water St.
Dobson, William M., now Battle Creek, Mich., U. S. Vets. Bureau Hosp. No. 100.

Dubins, Joseph A., Dorchester, from Glenway St. to 103 Columbia Rd.

Dunham, Henry B., Trenton, N. J., from 619 Stuyvesant Ave. to 923 Edgewood Ave.

Dunham, Rand A., from Easton, Me., to East Millocket, Me.

Eidam, Carl H., from Lawrence to Methuen, office Lawrence, 334 Prospect St.

Elkind, Henry B., Allston, office now Boston, 5 Joy St.
Galleani, Ilia, from Somerville (Middlesex South) to Boston (Suffolk), 483 Beacon St.

Gay, William M., from Tupper Lake, N. Y., to Saranac Lake, N. Y., 31 Pine St.

Giddings, Harold G., Newton Center, Boston office from 520 to 270 Commonwealth Ave.

Greene, Isadore, from Hathorne (Essex South) to Roxbury (Norfolk), office Boston, 68 Bay State Rd.

Harriman, Perley, Lynn, from 290 Summer St. to 11 Atlantic St.

Haxt, Joseph S., from Medical Corps, U. S. Army, to Burlingame, Calif., 1515 Hillside Drive.

Hooper, George H., from Brockton (Plymouth) to Tampico, Mexico (Non-Resident List), Wm. C. Gorgas Hosp.

Hughes, Edgar H., from Greenfield (Franklin) to Brooklyn, N. Y. (Non-Resident List), 9 Webster Ave.

Hutchinson, Claribel M., from Boston (Suffolk) to Waltham (Middlesex South), 244 School St.

Inman, William C., from Salem (Essex South) to Worcester (Worcester), Worcester City Hosp.

Johnson, Herbert Lewis, Hadley, from Main St. to 3 West St.

Mella, Hugo, from Boston (Suffolk) to Denver, Colo. (Non-Resident List), Medical Dept., University of Colorado.
Miller, John G., Jr., Lawrence, now 217 Jackson St. Mills, Alfred E., from Somerville, to Medford, 9 Wicklow Ave.
Monette, Camille J., from Williamansett (Hampden) to Plymouth, N. H. (Non-Resident List).
Monroe, Noel G., from Southbridge (Worcester) to Watertown (Middlesex South), office Boston, 39 Boylston St.
Papas, P. N., Boston, from 360 to 467 Commonwealth Ave.
Parker, Charles C., Jr., Roxbury, from 425 Warren St. to 2 Humboldt Ave.
Pettingill, Warren M., from Lawrence to Methuen, 70 Broadway.
Simmons, James G., from Worcester (Worcester) to Fitchburg (Worcester North), 30 Myrtle Ave.
Spooner, Lesley H., from Boston (Suffolk) to Brookline (Norfolk), office Boston, 520 Commonwealth Ave.
Stetson, Frederick W., has removed his office from 483 Beacon St. to 144 Commonwealth Ave., Boston.
Thompson, Richard H., Malden, from 72 Washington St. to 156 Hawthorne St.
Thorndike, Townsend W., has moved from Boston (Suffolk) to Cambridge (Middlesex South), office Boston, 475 Commonwealth Ave.
Trainor, John B., Fall River, from 1515 to 1517 South Main St.
Wheeler, LeRoy R., Boston, from 35 Bay State Rd. to 472 Commonwealth Ave.
1919-1925 Woody McIver, Springfield, 248 Pearl St. Readmitted by Censors, May 7, 1925.
Workman, W. Hunter, from Worcester (Worcester) to Newton (Middlesex South), 300 Franklin St.

MISCELLANY

RESULT OF THE MAY, 1925, EXAMINATION CONDUCTED BY THE BOARD OF REGISTRATION IN MEDICINE

REGISTERED JUNE 4, 1925

Andrews, John Raymond, House of Mercy Hospital, Pittsfield, Mass.
Burch, Harry Moffett, N. Y. Ophthalmic Hospital, 23rd and 3rd Ave., New York, N. Y.
DeKruif, Mary Fisher, Wellesley College, Wellesley, Mass.
Dodd, Katherine, 74 Fenwood St., Boston, Mass.
Dublin, Katherine Joseph, 34 Berkeley St., Lawrence, Mass.
Emery, Ruth, 130 Elm St., Saco, Me. (Apt. Pelham).
Franks, Helen Lucile Williamson, 1152 Commonwealth Ave., Boston, Mass.
Hough, Garry de Neuville, Jr., 172 23rd St., Jackson Heights, L. I.
Hrabra, Jennie, 19 W. 101st St., New York, N. Y.
McKenzie, Wilfred Lawrence, 10 Symmes Rd., Winchester, Mass.
Merican, Milton, 149 W. Tremont St., Bronx, N. Y.
Pickwick, Harold Curtis, Lisbon, N. H. (Box 3).

REJECTED JUNE 4, 1925

Middlesex 1923-23-24-25.*
Univ. Catania, Italy, 1917.
Naples Univ. 1914.
Athens 1923.
Mass. Ost. 1925-25.
St. Louis P. and S. 1921-22-22-22-23-23-24-24.
Kansas City College of Medicine and Surgery 1922.
Maryland 1913.

*The figures give the year of graduation of the rejected applicants.

Whole number examined, 33. Registered, 12. Rejected, 21.

MEXICO PLANS HEALTH CAMPAIGN

An extensive health campaign is to be undertaken in Mexico City according to a recent announcement. The program has been laid out by the National Academy of Medicine and the Child Welfare Association. Three thousand children died in Mexico City during May according to statistics. The toll is heaviest from May to September. During the campaign milk will be carefully inspected and instruction in hygiene given. There will be centres of instruction for mothers, also free medical service and inspection of homes. Owners of homes will be obliged to take proper sanitary precautions.

UNMARRIED MOTHERS AND THEIR BABIES

DECREASED infant mortality, fewer commercial agencies profiting from the unfortunate situation of unmarried mothers, fewer abandoned babies—these were found by the United States Children's Bureau to be some of the results of the Maryland law forbidding, except under special conditions, the separation of mother and baby for the difficult first six months of the baby's life.

Most striking was the enormous saving in baby lives apparently due to the law. In 1915 one out of every 3 babies of unmarried mothers died during the first year of life, and 1 out of every 4, during the first six months. In 1921, only 1 out of every 8 died during the first year, and only 1 in every 12 during the first six months. The reduction in infant mortality was more than 50 per cent. During the same period the rate for infants of legitimate birth was reduced less than 20 per cent. In 1915 illegitimate babies died at a rate three times as high as the rate for infants born in wedlock; in 1921 at a rate only one-and-a-half times as high.

The decrease in mortality from gastric and intestinal diseases among the illegitimate babies was great, particularly during the early months of the first year. This, the bureau believes, may be the result of the increase in breast feeding made possible because the mothers and babies were kept together.

In order to discover the effect of the law upon agencies caring for the unmarried mother or her baby, 24 hospitals, social agencies, and maternity homes in Baltimore were visited. Twenty of these had been engaged in social service affecting the illegitimacy problem both before and after the law became effective. In 13 of the 20, it was found, no changes were evident in the methods of dealing with the unmarried mother and her baby. The other 7 had adopted policies which were the direct result of the operation of the law. Before the passage of the law their plans of work were varied. Some of them accepted babies of any age on

surrenders signed by the mothers. Some of the hospitals arranged that mothers would not see their babies; some hospital superintendents placed advertisements in the newspapers offering the babies for adoption. Sometimes surrenders of their children were signed by mothers before the children were born.

Another result of the law seems to be that fewer unmarried mothers come from States other than Maryland to Baltimore for the birth of their babies. It was also found that, in spite of the fear that the law would lead to an increase in the number of babies abandoned, the number of foundlings during the year preceding the passage of the law was 23 while the number in 1923 was 6.

A very important feature of the Maryland law, the Children's Bureau points out, is its provisions for regular proceedings, and formal records, in cases where separation of a baby from his mother for placement in a foster home or institution is desired. Such separation is not permitted except in one of three ways: On the signing of certificates by two qualified physicians stating that the separation is necessary for the physical good of the mother or of the child, and setting forth the reasons for this necessity; by direction of the Board of State aid and charities; or by order of a court of competent jurisdiction. A record must be kept of the institution or home in which the baby is placed.

RECENT DEATHS

GALLIGAN.—Dr. EUGENE THOMAS GALLIGAN, a retired member of the Massachusetts Medical Society, died at his home in Roxbury, June 4, 1925, at the age of 68.

Dr. Galligan was born in Taunton, June 26, 1856, was graduated from Harvard Medical School in 1882, and joined the State medical society. He settled in practice in Roxbury, was physician to the House of the Angel Guardian and enjoyed a large practice.

ROBINSON.—Dr. LUCY ROBINSON, for more than 40 years a practising physician in Brockton, died June 12, 1925, at her home in that city, aged 85. She was born in Middleboro, daughter of Dr. and Mrs. Morrill Robinson. Of delicate health when a child, it was feared she would develop tuberculosis, but her father insisted on her living an out-of-door life, and her health was restored. Her education was delayed, and it was not until 1885 that she entered the Woman's Medical College in Pennsylvania at Philadelphia, and was graduated in 1888 at the age of 48.

She began practice in Brockton and joined the Massachusetts Medical Society in the same year, devoting herself largely to gynecology. In 1915 her name was placed on the retired list.

She was always interested in the Brockton Hospital, and when it was founded in the early '90s she was a member of the board of trustees and auditor for many years. She was a member of the Warren Avenue Baptist Church, Plymouth County Medical Society, and the New England Hospital Society.

HAYS.—Dr. I. MINIS HAYS, widely known physician and for many years secretary of the American Philosophical Society, died recently at his home in Philadelphia.

CORRESPONDENCE

THE CANCER PROBLEM

Editor, Boston Medical and Surgical Journal:

How many cases of cancer are there in Massachusetts and how adequate is the care available to them? We know the number of cancer deaths, but not the number of cancer cases. Adequate care of these includes diagnostic, operative, X-ray and radium service as well as institutional beds for certain of the inoperables. Are all of these services reasonably available? If not, give concrete instances.

Definite forms of inadequate treatment are the "cancer cures" and various cults. The patient may put his faith in these during the all-important and all too short period when a competent operation may possibly effect a cure. To what extent is the volume of inoperable cancer in Massachusetts being swelled in this way?

By a Legislative resolve the Departments of Public Health and Public Welfare, jointly, have been directed to study the whole cancer problem, with especial reference to institutional service for the inoperables, and, if indicated, to suggest means of extending the same. Few problems are more baffling or more urgent from a humanitarian and economic standpoint. We, therefore, solicit all possible facts and suggestions bearing on this subject. Letters should be addressed to the Department of Public Health, State House, Boston.

Yours truly,

JOHN H. NICHOLS, *Chairman*,

MERRILL E. CHAMPION,

FRANK W. GOODHUE,

GEORGE H. BIGELOW, *Secretary*,

Joint Committees of the Departments of Public Welfare and Public Health.

AN UNUSUAL CASE OF RECTAL IMPACTION

June 4, 1925.

Editor, Boston Medical and Surgical Journal:

The following described condition is probably unusual and worthy of notice.

A few days ago Mrs. M.— visited my office complaining that she was unable to move her bowels. As it was late in the evening she was taken to the hospital and was given an s.s. enema. The nurse reported good results.

Two days later I was called to Mrs. M.—'s home. She was crying and otherwise very nervous, and said there was a constant desire to defecate, but she could pass nothing. Rectal examination was made. The whole rectum seemed to be filled with a soft mass, but the consistency was unlike feces. A portion was removed and found to be bran flour. A half pound of bran flour was removed manually.

This was followed by rectal irrigation until the return flow was clear. It is safe to say that nearly a half pound was washed away.

Upon questioning her it was found that she had been desirous of reducing her weight and for this purpose had been subsisting on a diet of five to six bran muffins each meal with a little tea or coffee.

THEODORE L. STORY, M.D.

Holden, Mass., June 4, 1925.

FURTHER FACTS RELATING TO THE FUNCTIONS OF THE INDUSTRIAL ACCIDENT BOARD

Editor, Boston Medical and Surgical Journal:

Dr. T. K. Richards is to be commended for publishing his report (see B. M. AND S. J., June 4) of "A Legal Decision Concerning a Physician and the Massachusetts Workmen's Compensation Act," and congratulated on his successful outcome.

Although I do a relatively large amount of industrial accident work for one engaged in special practice, yet I have so far had nothing but the most amicable relations with the insurance companies, and my only disagreeable experience has been this same arbitrary attitude on the part of the Industrial Accident Board in reducing the amount of compensation for physicians' services.

Mine was a case of an elderly man employed by a town at its stone crusher. Fifteen or more years previously he had lost the sight of one eye through accident and while at work was struck in the other eye by a piece of stone, and three days later he was brought to my office by a fellow town employee. There being a relatively large central infected corneal ulcer well established, the serious possibility was recognized, he was sent to a local hospital and the superintendent of streets called in and my action received official sanction. Bacteriological examination verified a clinical diagnosis of serpent ulcer, and it seemed wise to keep in close contact with the progress of the disease. Eventually the eye was lost through pan ophthalmitis and the globe enucleated. Those who have had similar experiences will understand the gravity and anxiety associated with the care of such a case, and appreciate one's feelings when one or more laymen attempt to transmute the effort into dollars and cents.

Although the town in question insures itself, the same scale of fees was applied in rendering a bill as was used when an insurance company assumed the hazard, and so far has not been questioned by any of those companies. The Board of Selectmen took exception to the total of my bill, filed a protest with the Industrial Accident Board without consulting me, a hearing was held by one of the members of the Board, and a decision making a substantial cut in my fees was rendered.

I turned the matter over to a competent firm of attorneys and they expressed an opinion to the effect that the Industrial Accident Board had practically arbitrary power in its decisions on fees, and that they (the attorneys) had been unable to find a record of any of their decisions not being upheld by a court of equity. So I took my loss, and since then have had an increasing wonder at the ease with which we humans, when grouped together as Boards, set up standards and render decisions upon subjects with which we have had little if any practical experience.

In view of the relatively large amount of industrial accident work the members of the Massachusetts Medical Society do in the course of a year it has seemed to me that a legal aid department—other than that relating to malpractice matters—could be established by the Council and be the means of not only rendering material assistance but do a bit towards a better welding of our membership.

(My apologies if this suggestion makes the keepers of our Society wampum a little restless or uneasy.)

Yours truly,
B. P. CROFT.

Greenfield, Mass., June 5, 1925.

CONNECTICUT DEPARTMENT OF HEALTH

MORBIDITY REPORT FOR THE WEEK ENDING

JUNE 6, 1925

Diphtheria	34	Last week	171
Last week	17	Typhoid fever	3
Diphtheria bacilli		Last week	7
carriers	17	Chickenpox	82
Whooping cough	150	Encephalitis epid.	1
Last week	83	German measles	40
Scarlet fever	66	Influenza	4
Last week	67	Mumps	56
Measles	366	Pneumonia (broncho)	17

Pneumonia (lobar)	29	Tuberculosis (other forms)	1
Tetanus	1	Gonorrhea	21
Tuberculosis (pul.)	31	Syphilis	21

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

DISEASES REPORTED FOR THE WEEK ENDING

JUNE 6, 1925

Anterior poliomyelitis	1	Pellagra	2
Chickenpox	193	Pneumonia, lobar	75
Diphtheria	100	Scarlet fever	219
Dog-bite requiring anti-tropic treatment	8	Septic sore throat	2
Encephalitis lethargica	2	Syphilis	39
Epidemic cerebrospinal meningitis	1	Suppurative conjunctivitis	21
German measles	359	Tetanus	2
Gonorrhea	95	Trachoma	4
Hookworm	2	Trichinosis	4
Influenza	8	Tuberculosis, pulmonary	130
Measles	888	Tuberculosis, hilum	40
Mumps	55	Typhoid fever	5
Ophthalmia neonatorum	22	Whooping cough	140

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

RESUME OF COMMUNICABLE DISEASES

MAY, 1925

GENERAL PREVALENCE

The only common communicable diseases showing an increase during May were German measles and whooping cough.

	May, 1925	April, 1925	May, 1924
German measles	1,157	1,019	370
Whooping cough	664	622	378

RARE DISEASES

Anterior poliomyelitis was reported from Boston, 1.

Dog-bite requiring anti-tropic treatment was reported from Amesbury, 1; Arlington, 2; Billerica, 3; Boston, 3; Lawrence, 1; Lowell, 6; Lynn, 1; Newton, 2; Peabody, 18; Swampscott, 1; Winthrop, 1; total, 38.

Dysentery was reported from Medford, 1.

Encephalitis lethargica was reported from Beverly, 2; Boston, 5; Brockton, 1; Fall River, 2; Haverhill, 2; Lynn, 1; Waltham, 1; Worcester, 2; total, 16.

Epidemic cerebrospinal meningitis was reported from Boston, 2; Clinton, 1; Concord, 1; Fall River, 1; Holyoke, 1; Ipswich, 1; Lowell, 1; Northfield, 1; Salem, 1; Upton, 1; Worcester, 1; total, 12.

Hookworm was reported from Boston, 3.

Septic sore throat was reported from Boston, 12; Hubbardston, 1; total, 13.

Smallpox was reported from North Attleboro, 1.

Tetanus was reported from Lowell, 1.

Trachoma was reported from Boston, 4; Lawrence, 1; Milford, 1; total, 6.

DISTRIBUTION

All Communicable Diseases

	May, 1925	May, 1924
Total cases (all causes)	9,985	9,998
Case rate per 100,000 population	247.4	249.8

Certain Prevalent Diseases

			May,	May,
Diphtheria			1925	1924
Total cases			351	559
Case rate per 100,000 population			8.7	14.0
Cities and towns noticeably exceeding their median endemic indexes*:				
Quincy	(7)	25	Stoneham	(2) 21
Measles			May,	May,
Total cases			1925	1924
Case rate per 100,000 population			3,756	3,355
Cities and towns noticeably exceeding their median endemic indexes*:				
New Bedford	(6)	147	Stoneham	(5) 32
Dedham	(2)	24	Andover	(4) 54
Framingham	(13)	35	Ashby	(19) 53
Hopkinton	(0)	8	Lawrence	(120) 179
Norwood	(3)	35	Lowell	(23) 79
Quincy	(224)	269	Methuen	(42) 67
Haverhill	(5)	54	Somerville	(104) 136
Melrose	(13)	226	Winchester	(1) 102
Merrimac	(0)	24		
Scarlet Fever			May,	May,
Total cases			1925	1924
Case rate per 100,000 population			996	1,447
Cities and towns noticeably exceeding their median endemic indexes*:				
Fall River	(19)	30	Salem	(8) 17
Franklin	(0)	6	Swampscott	(2) 10
Natick	(3)	10	Chicopee	(1) 9
Norwood	(2)	14	Springfield	(30) 82
Beverly	(4)	11	W. Springfield	(2) 8
Peabody	(4)	12	Greenfield	(3) 13
Tuberculosis, Pulmonary			May,	May,
Total cases			1925	1924
Case rate per 100,000 population			594	553
			14.7	13.88
Tuberculosis, Other Forms			May,	May,
Total cases			1925	1924
Case rate per 100,000 population			92	101
			2.3	2.5
Typhoid Fever			May,	May,
Total cases			1925	1924
Case rate per 100,000 population			37	44
			.91	1.1
Whooping Cough			May,	May,
Total cases			1925	1924
Case rate per 100,000 population			664	378
			16.4	9.4
Cities and towns noticeably exceeding their median endemic indexes*:				
Dartmouth	(0)	8	Andover	(2) 24
Mansfield	(0)	46	Arlington	(2) 8
Cambridge	(30)	58	Templeton	(0) 35
Newton	(20)	61	Springfield	(17) 51
Quincy	(11)	48		

*The median endemic index is obtained by arranging in arithmetical sequence the monthly totals of reported cases for the past five years and selecting the middle figure. The numbers in parentheses after the name of each city and town indicate the median endemic index for that city or town; the numbers without parentheses indicate the cases reported during the current month.

NEWS ITEMS

TUFTS COLLEGE COMMENCEMENT—Monday morning, June 15, marked the sixty-ninth annual commencement at Tufts College. The exercises were held out of doors under the beautiful old trees on the college campus at Medford Hillside. One hundred and four candidates were awarded the degree of Doctor of Medicine, including one Summa Cum Laude and twenty-three Cum Laude. The Summa Cum Laude was awarded to Louis Eisenhardt, William McKinley Roberts, valedictorian, delivered an oration entitled "Insulin as a Cure for Diabetes."

MEETING OF THE N. E. BOARDS OF MEDICAL REGISTRATION—A Federation of the New England Medical Boards of Registration has existed for many years. The meeting this year was in Providence and was addressed by Dr. W. C. Woodward of Chicago. His topic was "A Model Registration Act."

ANNOUNCEMENT—Dr. Wyman Richardson announces the opening of his office at 270 Commonwealth Avenue, Boston.

THE DRIVE FOR FUNDS FOR THE WORCESTER MEMORIAL HOSPITAL—In last week's issue mention was made of the extraordinary success of this drive. Subsequent reports are to the effect that over seven hundred thousand dollars have been subscribed.

FOOD LAW VIOLATIONS—Dr. Harvey W. Wiley is reported to have alleged that the pure food law which was created in Congress under his guidance is not being obeyed. He specifies the use of sulphur dioxide and sulphates, benzolic acid and benzoates in the preparation of so-called embalmed beef. Also that alum is used in the making of bread and preservatives added to pickles.

The customs complained of, it is alleged, have been permitted because executive orders by Secretaries of Agriculture since 1907 have nullified the provisions of law.

EXPERTS TO STUDY ETHYL GAS—Seven persons have been appointed by Surgeon-General Cummings to study the dangers of tetra-ethyl lead and report before January, 1926.

These persons are Dr. David L. Edsall, Dr. W. H. Howell, Dr. A. J. Chesley, Dr. Reid Hunt, Dr. Walter Leathers, Dr. Julius Steiglitz and Professor Charles Amory Winslow.

THE OFFICERS ELECTED AT THE ANNUAL MEETING OF THE NEW ENGLAND DIVISION OF THE AMERICAN NURSES' ASSOCIATION: President, Miss Sally Johnson, superintendent of the Training School for Nurses at the Massachusetts General Hospital; vice-president, Miss Lucy C. Ayer, superintendent of the Woonsocket Hospital; secretary, Miss Esther Dart, matron of the Stillman Infirmary, Cambridge; treasurer, Miss Ednah A. Cameron, secretary of the State Board of Nurse Examiners, Concord, N. H.

ILLNESS DUE TO VACCINATION—Some time since, publicity was given to a suit against the Cunard Steamship Company by a passenger who claimed to have suffered from vaccination.

It appears that the plaintiff sailed from Cherbourg in 1920. Before embarking he was vaccinated by a French physician who was paid by the company. It was claimed that the plaintiff was vaccinated against his will and used violence while the operation was performed and that he suffered a condition known as traumatic neuritis.

It was shown that the vaccination area was covered with a shield. The ship's surgeon believed that the shield had been disarranged and that the patient may have infected the lesion. Dr. Lusk, who cared

for the patient in New York, testified that the patient had a cellulitis and not erysipelas. Considerable pus was evacuated by means of incisions. Dr. Lusk contended that no permanent injury followed and that the extent of the injury was exaggerated.

Another argument against the use of shields!

OFFICERS OF THE MASSACHUSETTS STATE NURSES' ASSOCIATION—The officers of this association elected for 1925-1926 are: President, Miss Jessie E. Catton, superintendent of the New England Hospital for Women and Children; vice-president, Miss Sally M. Johnson, superintendent of the Nurses' Training School of the Massachusetts General Hospital; recording secretary, Miss Mary A. McMahon, superintendent of Nurses, Boston State Hospital; corresponding secretary, Miss Helen M. Blaisdell, instructor at the Peter Bent Brigham Hospital; treasurer, Miss Emma M. Nichols of West Roxbury.

REMOVAL—Dr. Douglas Graham has removed his office to his home, 177 Aspinwall Avenue, Brookline.

Dr. Douglas Graham reports attendance at fifty consecutive annual meetings of the Massachusetts Medical Society.

APPOINTMENT OF DR. JAMES GLASS—The vacancy caused by the death of Dr. George Bancroft of Natick, medical examiner for the Eighth Middlesex County District, has been filled by the appointment of Dr. James Glass of Framingham, who acted as associate examiner for the past six years.

AN UNUSUAL ACCIDENT—It is reported that a Delaware River diver working about 40 feet under water was overcome by heat. The cause of the overheated atmosphere was due to the heating of the air pump, which was exposed to the abnormal temperature of June 6 last. Fortunately he was rescued, although unconscious when brought to the surface. It was estimated that the temperature in the diving suit exceeded 115 degrees.

REPORTS AND NOTICES OF MEETINGS*

BOSTON MEDICAL HISTORY CLUB

ANNUAL MEETING, APRIL 27, 1925

DR. A. WARREN STEARNS talked informally on "Dr. Joseph Foster" who practiced in Billerica, Mass., 1806-1810. He was born in Canterbury, N. H., 1779, and received his education, partly at the Noyes School in Concord, N. H., and partly in Cambridge, taking courses in medicine under John Warren and others. Dr. Stearns has a large collection of his notes, bills, medicines, and clothes, some of which he demonstrated. The notes were on a wide range of subjects, including cures, diabetes, gunpowder, and shoe-blacking. Although Dr. Foster is not mentioned in the "History of the Massachusetts Medical Society," Dr. Stearns was able to show his certificate of membership signed by John Warren. Dr. Stearns was dressed in clothes formerly belonging to Dr. Foster, including breeches, cutaway coat, plush waistcoat, and high hat, all of which are in an excellent state of preservation. He also exhibited Dr. Foster's medical box.

Dr. William P. Coues read on "Flaubert's Madame Bovary." Flaubert, whose father was Surgeon-in-Chief at the hospital in Rouen, was born in 1821. He did not learn to read until nine, became an author against his father's wishes, suffered from epilepsy all his life, was aloof, eccentric, and high-tempered, but wrote with meticulous care and had a splendid insight into medicine and surgery. The book, Madame Bovary, is a series of pictures of remarkable reality. An unsuccessful operation for clubfoot is described in detail, specially interesting being the account of the subsequent amputation for gangrene by a consulting surgeon. Dr. Coues read abstracts and commented upon various passages in the novel.

Dr. E. W. Taylor spoke informally on "Witches Confession." The period of Salem witchcraft lasted only a few months in 1692. About twenty witches were executed and fifty more confessed to be witches, but were later freed from prison. Most of the so-called confessions were forced, either as a means of saving the suspected person's life, or because confession on the part of the witch was urged by their families. Those who at first protested and pleaded innocence were forced to admit their guilt by "third degree" methods of examination. Dr. Taylor spoke in particular of the confession of Abigail Hobbs, a woman of the vagabond type who could neither read nor write. He showed a photostat copy of her confession dated April 19, 1692.

Dr. Isadore Coriat showed a number of books and papers relating to witchcraft. He suggested that, in his opinion, witchcraft was often based on the terror of castration,—a castration anxiety neurosis.

Dr. Edward C. Streeter reported his observations at the Britwell Court Library Sale, recently held in London. Exceptionally high prices were paid for early English imprints, many of which were bought for Americans. He reported a few purchases for the Boston Medical Library.

ANNUAL MEETING OF MALDEN ANTI-TUBERCULOSIS SOCIETY, INC.

THE annual meeting of the Malden Anti-Tuberculosis Association was held at the Malden Health Center on Tuesday evening, June 2. Following the formal business of annual reports the election of officers for the coming year was in order, resulting in this list:

President—Hon. George Louis Richards.

Vice-Presidents—Dr. William H. McBain, Robert A. Hodgdon and Dr. Samuel Hoberman.

Treasurer—J. Elliot Knowlton.

Secretary—F. Anne Green.

Directors for three years—Edward R. Berry,

*Notices of meetings must reach the JOURNAL office on the Friday preceding the date of issue in which they are to appear.

Ph. D., William E. Downer, Mrs. Joseph Hogg and Philip Wheeler.

The Directors who hold-over for one year or two years are: Mrs. Victor Bychower, Joshua T. Day, Ernest A. Glidden, Charles Keniston, Jr., Dr. Charles D. McCarthy, Mrs. Honora Moriarty, Mrs. Michael Mulvey, Monsignor Richard Neagle, Dr. Charles E. Prior and John Ritchie.

There were two speakers, Dr. Samuel Hoberman, whose subject was, "The Reasons for Complete Periodic Physical Examinations," and John Ritchie, whose topic was, "Place of Non-official Agencies in Health Work."

AMERICAN DIETETIC ASSOCIATION

The yearly convention of the American Dietetic Association will be held at the Edgewater Beach Hotel, Chicago, Ill., on October 12, 13, 14 and 15, 1925.

The program, which is being arranged by Dr. Kate Daum of New York City, aims to cover the varied activities of the association, so that all who are concerned with the food problem in any of its phases will find something of especial interest to them.

The first three days will be devoted to the program and the exhibits, the latter being of both a commercial and non-commercial nature. The fourth day will be given over to sightseeing. A series of trips is being planned to show the practical application of theory and science in the various fields of dietetic activities. You will have an opportunity to visit the Sarah Morris Hospital for Children. It has a thoroughly modern and well-equipped milk laboratory. You may see the various types of infant foods used in the process of preparation.

An opportunity will be given to see the extensive results that have been accomplished by the infant welfare organization of Chicago. Some of the stations will be open for your inspection.

BOOK REVIEWS

Abt's Pediatrics. Volume VI. Edited by ISAAC A. ABT, M.D., Professor of Diseases of Children, Northwestern University Medical School, Chicago; Attending Physician, Sarah Morris Hospital for Children of Michael Reese Hospital, Chicago. Philadelphia and London. W. B. Saunders Co.

The present volume of Abt's Pediatrics is a particularly valuable one, largely on account of the immense amount of text on the infectious diseases, such as have not already been considered in a previous volume. The opening chapter is on body temperature and its regulation, by Dr. Fitz B. Talbot, an authority on the subject.

Typhoid and paratyphoid fevers are discussed by Dr. J. H. Mason Knox, Jr., typhus fever and Asiatic cholera by Victor G. Heiser, acute rheumatic fever by Maynard Ladd, diphtheria by Park and Dickson of New York, whooping cough by Friedlander, who recommends the use of vaccines, and measles, rubella and Filatow-Duke's (Fourth) Disease by Charles Herrmann. Epidemic meningitis is

unusually well treated by Josephine B. Neal of the New York Department of Health, and hydrophobia by Anna W. Williams. It is unfortunate that in the chapter on scarlet fever by George H. Weaver no mention could have been included of the recent important work by Dochez and the Dicks.

Considerable space has been devoted to anesthesia with a description of the use of ethylene, excellent except that the very great danger of combustion has not been sufficiently emphasized. The volume ends with chapters on the peculiarities of surgery in childhood, fetal malformations, vulvovaginitis and arthritis deformans.

From Infancy to Childhood. By RICHARD M. SMITH, M.D., Assistant Professor of Child Hygiene, Harvard University; Associate Physician, Children's Hospital, Visiting Physician, Infants' Hospital, Boston. The Atlantic Monthly Press, Boston.

Dr. Smith in this new small book stresses the importance of the periodic health examination, the basis on which much of the practice of medicine of the future will rest. The physical and mental development, training and education of the growing child are all touched upon, even if somewhat superficially, for the benefit of mother and nurse. A certain amount of practical information is given. The book is short and it is superficial, and perhaps for these very reasons best suited for the readers it is intended to reach. One might wish that some time Dr. Smith would dig more deeply into his fund of experience and knowledge and write for his fellow practitioners as well as for doting mothers.

Diseases and Deformities of the Foot. By JOHN JOSEPH NUTT, B. L., M. D., F. R. C. S. Second Edition Completely Revised. New York: E. B. Treat & Company, 1925.

As said in the preface to the First Edition, this is a book which is prepared for physicians. The chapters on the anatomy, physiology, and examination will be very helpful to the general practitioner in giving a definite method of approaching foot conditions. The rest of the book deals with conditions such as weak foot, flat foot, congenital club foot, infantile paralysis, tuberculosis, and other ailments.

In reading the second edition of this book, it must be remembered that the author is expressing his own ideas and those of the community in which he works and that he does not give the experience of other orthopaedic surgeons. This has its advantages, in that it varies from some books which, in their attempt to give the opinions of the many, fail to give the reader what the author himself believes,—and is not this latter what one wishes to find in a book?